TOXICOLOGICAL PROFILE FOR
1,2-DICHLOROPROPANE

Agency for Toxic Substances and Disease Registry (ATSDR)
U.S. Public Health Service

In collaboration with
U.S. Environmental Protection Agency (EPA)

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DISCLAIMER

Mention of company name or product does not constitute endorsement by the Agency for Toxic Substances and Disease Registry.

FOREWORD

The Superfund Amendments and Reauthorization Act of 1986 (Public Law 99-499) extended and amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law (also known as SARA) directed the Agency for Toxic Substances and Disease Registry (ATSDR) to prepare toxicological profiles for hazardous substances which are most commonly found at facilities on the CERCLA National Priorities List and which pose the most significant potential threat to human health, as determined by ATSDR and the Environmental Protection Agency (EPA). The lists of the most significant hazardous substances were published in the Federal Register on April 17, 1987, and on October 20, 1988.

Section 110 (3) of SARA directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list. Each profile must include the following content:

> (A) An examination, summary and interpretation of available toxicological information and epidemiological evaluations on the hazardous substance in order to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects,
>
> (B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure which present a significant risk to human health of acute, subacute, or chronic health effects, and
>
> (C) Where appropriate, an identification of toxicological testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans.

This toxicological profile is prepared in accordance with guidelines developed by ATSDR and EPA. The original guidelines were published in the Federal Register on April 17, 1987. Each profile will be revised and republished as necessary, but no less often than every 3 years, as required by SARA.

The ATSDR toxicological profile is intended to characterize succinctly the toxicological and health effects information for the hazardous substance being described. Each profile identifies and reviews the key literature that

describes a hazardous substance's toxicological properties. Other literature is presented but described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.

Each toxicological profile begins with a public health statement, which describes in nontechnical language a substance's relevant toxicological properties. Following the statement is material that presents levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine a substance's health effects is described in a health effects summary. Data needs that are of significance to protection of public health will be identified by ATSDR, the National Toxicology Program of the Public Health Service, and EPA. The focus of the profiles is on health and toxicological information; therefore, we have included this information in the front of the document.

The principal audiences for the toxicological profiles are health professionals at the federal, state, and local levels, interested private sector organizations and groups, and members of the public. We plan to revise these documents as additional data become available.

This profile reflects our assessment of all relevant toxicological testing and information that has been peer reviewed. It has been reviewed by scientists from ATSDR, EPA, the Centers for Disease Control, and the National Toxicology Program. It has also been reviewed by a panel of nongovernment peer reviewers and was made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.

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Agency for Toxic Substances and
Disease Registry

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1. PUBLIC HEALTH STATEMENT

1.1 WHAT IS 1,2-DICHLOROPROPANE?

1,2-Dichloropropane is a colorless liquid belonging to a class of chemicals called volatile organic compounds (VOCs). It has a chloroform-like odor and evaporates quickly at room temperature. It is a man-made chemical and people are probably responsible for all releases of 1,2- dichloropropane into the environment. 1,2-Dichloropropane is now used in the United States only in research and industry. Before the early 1980s, 1,2-dichloropropane was used in farming as a soil fumigant and was found in some paint strippers, varnishes, and furniture finish removers. Most of the 1,2-dichloropropane released into the environment finally ends up in the air or groundwater. When applied to soil in one experiment, all but 1% dispersed in 10 days. Breakdown in both the air and groundwater is slow. The rate at which a chemical breaks down is usually explained by how long it takes for half the chemical to disappear (half-life). The half-life of 1,2- dichloropropane in air is not known exactly, but it is longer than 23 days, which means that 1,2-dichloropropane can spread to areas far from where it is released. In groundwater, the half-life of 1,2-dichloropropane is estimated to be between 6 months and 2 years. For more information refer to Chapters 4 and 5 of this document.

1.2 HOW MIGHT I BE EXPOSED TO 1,2-DICHLOROPROPANE?

Air levels of 1,2-dichloropropane are usually quite low. In city areas of the United States, the average amount in air is about 22 parts per trillion (ppt). 1,2-Dichloropropane is found in a few drinking water supplies, and most of those are from groundwater sources. A nationwide survey of groundwater supplies showed that 1.4% of these supplies contained 1,2-dichloropropane levels at around 1 part per billion (ppb). The highest amount of 1,2-dichloropropane in the survey was 21 ppb. Private wells in farming areas where 1,2-dichloropropane was once used as a soil fumigant have the greatest risk for contamination. Occupational exposure to 1,2-dichloropropane may result during its production, its use in chemical reactions and as an industrial solvent, and evaporation from wastewater that contains the chemical. Workers involved in cleaning up hazardous waste or spill sites that contain 1,2-dichloropropane may also be exposed. A national survey conducted by the National Institute for Occupational Safety and Health (NIOSH) in 1981-1983 estimated that 2119 workers outside of the farming sector were exposed to 1,2-dichloropropane. Use of this chemical has recently decreased very much, however, so that the number of exposed workers may now be much lower. According to industry spokesmen, levels of exposure among exposed workers range from less than 1 part per million (ppm) to less than 25 ppm, depending on the industry. 1,2-Dichloropropane was found in 26 of the 1177 hazardous waste sites on the National Priority List (NPL) and gases from these sites may contain low levels of 1,2-dichloropropane. For more information on levels of 1,2-dichloropropane in

the environment and potential exposure to it, please refer to Chapter 5 of this document.

1.3 HOW CAN l,2-DICHLOROPROPANE ENTER AND LEAVE MY BODY?

1,2-Dichloropropane can enter the body if a person breathes air or drinks water contaminated with it, or if a person's skin comes in contact with it. If 1,2-dichloropropane is present at a waste site near homes that use wells as a source of water, the well water could be contaminated. A route of major exposure in the past was by accidentally or intentionally drinking cleaning products that contained 1,2-dichloropropane, but these cleaning materials are no longer produced in the United States. Experiments with animals have shown that when 1,2-dichloropropane enters the body through eating or drinking, it is quickly removed in the urine and feces and by the lungs when the animal breathes out. 1,2-Dichloropropane may enter the lungs of workers exposed where it is used indoors as a solvent. If 1,2-dichloropropane is released at a waste site and evaporates into the air, a person may breathe in 1,2-dichloropropane for a short time before it disperses. When the chemical was a part of some paint strippers, varnishes, and furniture finish removers, exposure of the skin through contact with these products occurred; however, the amount of 1,2-dichloropropane that entered through the skin is unknown. Soil around a waste site may be contaminated with 1,2-dichloropropane, but it is not known how much 1,2-dichloropropane enters the body through the skin upon contact with contaminated soil. For more information on how 1,2-dichloropropane enters and leaves the body, see Chapter 2.

1.4 HOW CAN 1,2-DICHLOROPROPANE AFFECT MY HEALTH?

Drinking 1,2-dichloropropane by humans (i.e., drinking cleaning solutions) has produced poisoning. At these high levels of exposure, effects include dizziness, headache, nausea, injury to the liver and kidneys, anemia, coma and, ultimately, death. Breathing high levels of 1,2-dichloropropane by humans, as in deliberate breathing of vapors from cleaning solutions, produces similar effects. No reports have been made of any health effects in humans following low-level exposure to 1,2-dichloropropane for either short or long time periods.

In animal experiments, low amounts of 1,2-dichloropropane breathed in over short- and long-term periods result in damage to the liver, kidney, and respiratory systems, while high amounts resulted in death. Short-term exposure to high levels of vapors also causes irritation to the eyes and throat. When 1,2-dichloropropane is given by mouth to animals over short- or long-term periods, damage to the liver and kidneys is seen at low doses, and death occurs at high doses.

1,2-Dichloropropane breathed or eaten for a short time has not been reported to produce cancer in humans, but long-term exposure by mouth in animals has produced evidence of liver cancer in mice and breast cancer in

female rats. The significance of the animal cancer studies to humans is not well understood. Irritation of the skin after contact with 1,2-dichloropropane has been seen in both humans and rabbits. 1,2-Dichloropropane has not been shown to cause birth defects in humans or animals, but a delay in the growth of bones has been seen in fetal rats following exposure of the mother rats. For more information on the health effects of 1,2-dichloropropane in humans and animals, see Chapter 2.

1.5 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO 1,2-DICHLOROPROPANE?

Tests are available to detect 1,2-dichloropropane in the urine and the blood. The available methods can predict the concentration of 1,2-dichloropropane in the air from levels in the urine, but not from levels in the blood. The levels of 1,2-dichloropropane in the urine, however, cannot predict specific health effects. The method for testing the urine is simple, but because special equipment is needed, the test is not yet routinely available. Because 1,2-dichloropropane leaves the body quickly, it is best to test for it soon after exposure. For more information on the medical tests available to detect exposure to 1,2-dichloropropane, see Chapter 2.

1.6 WHAT LEVELS OF EXPOSURE HAVE RESULTED IN HARMFUL HEALTH EFFECTS?

The amounts of 1,2-dichloropropane in air, drinking water and food that cause known health effects in humans and animals are shown in Tables l-l, l-2, l-3 and l-4. The idea of "dose-response" is important when assessing the effect of a chemical on humans or animals. Dose-response refers to the increase in adverse health effects that are observed as the amount of the chemical to which you are exposed increases. The exact amounts that result in the harmful effects in humans (see Section 1.4) are not known because no amounts of 1,2-dichloropropane were determined when the individuals were poisoned.

Minimal Risk Levels (MRLs) are included in Tables 1-l and l-3. These MRLs were derived from animal data for short-term and long-term exposure from breathing 1,2-dichloropropane and for short-term and longer-term exposure from eating or drinking 1,2-dichloropropane, as described in Chapter 2 and in Tables 2-l and 2-2. The MRLs provide a basis for comparison to levels which people might encounter either in the air or in food or drinking water. If a person is exposed to 1,2-dichloropropane at an amount below the MRL, it is not expected that harmful (noncancer) health effects will occur. Since these levels are based on information that it currently available, there is always some uncertainty associated with them. Also, since the method for deriving MRLs does not use any information about cancer, a MRL does not imply anything about the presence, absence, or level of risk of cancer.

1. PUBLIC HEALTH STATEMENT

TABLE 1-1. Human Health Effects from Breathing 1,2-Dichloropropane*

Short-term Exposure (less than or equal to 14 days)		
Levels in Air (ppb)	Length of Exposure	Description of Effects
		The health effects resulting from short-term exposure to air containing specific levels of 1,2-dichloropropane are not known.
50		Minimal Risk Level (derived from animal data, see Section 1.6 for discussion).
Long-term Exposure (greater than 14 days)		
Levels in Air (ppb)	Length of Exposure	Description of Effects
		The health effects resulting from long-term exposure to air containing specific levels of 1,2-dichloropropane are not known.
7		Minimal Risk Level (derived from animal data, see Section 1.6 for discussion).

*See Section 1.2 for a discussion of exposures encountered in daily life.

TABLE 1-2. Animal Health Effects from Breathing 1,2-Dichloropropane

Short-term Exposure (less than or equal to 14 days)		
Levels in Air (ppm)	Length of Exposure	Description of Effects*
100	14 days, 6 hr/day	Nasal damage in rats and mice.
480	10 hr	Death in mice.
1000	14 days, 6 hr/day	Nasal damage in rabbits.
1000	6-10 days, 7 hr day	Death in rats.
1500	9 days, 7 hr/day	Death in guinea pigs.
Long-term Exposure (greater than 14 days)		
Levels in Air (ppm)	Length of Exposure	Description of Effects*
15	13 weeks	Slight respiratory damage in rats.
150	13 weeks	Anemia in rabbit.
400	5 weeks	Death in mice.
1000	2-18 weeks	Death in rats, guinea pigs, and dogs.

*These effects are listed at the lowest level at which they were first observed. They may also be seen at higher levels.

TABLE 1-3. Human Health Effects from Eating or Drinking 1,2-Dichloropropane*

Short-term Exposure (less than or equal to 14 days)		
Levels in Food (ppm)	Length of Exposure	Description of Effects**
3.6		Minimal Risk Level (derived from animal data see Section 1.6 for discussion).
Levels in Water		The health effects resulting from short-term human exposure to drinking water containing specific levels of 1,2-di-chloropropane are not known.
Long-term Exposure (greater than 14 days)		
Levels in Food (ppm)	Length of Exposure	Description of Effects**
2.5		Minimal Risk Level (derived from animal data see Section 1.6 for discussion).
Levels in Water		The health effects resulting from long-term exposure to drinking water containing specific levels of 1,2-dichloropropane are not known.

*See Section 1.2 for a discussion of exposures encountered in daily life.

TABLE 1-4. Animal Health Effects from Eating or Drinking 1,2-Dichloropropane

Short-term Exposure (less than or equal to 14 days)		
Levels in Food (ppm)	Length of Exposure	Description of Effects*
2000	10 days	Mild nervous system effects in rats.
3850	14 days	Death in mice.
5000	10 days	Weight loss, anemia, and liver damage in rats.
10,000	10 days	Testicular damage in rats.
40,000	14 days	Death in rats.
Levels in Water		The health effects resulting from short-term animal exposure to drinking water containing specific levels of 1,2-di-chloropropane are not known.
Long-term Exposure (greater than 14 days)		
Levels in Food (ppm)	Length of Exposure	Description of Effects*
960	2 years	Liver damage in mice.
1900	2 years	Death in mice.
2000	13 weeks	Weight loss and anemia in rats.
2500	15 days	Slight effects on the growth of bones in fetal rats.
5000	2 years	Liver damage in rats.
5000	2 years	Death in rats.
Levels in Water		The health effects resulting from long-term animal exposure to drinking water containing specific levels of 1,2-dichloropropane are not known.

*These effects are listed at the lowest level at which they were first observed. They may also be seen at higher levels.

1. PUBLIC HEALTH STATEMENT

The Occupational Safety and Health Administration (OSHA) believes that 75 ppm 1,2-dichloropropane is acceptable for a normal 8-hour workday and a 40-hour workweek and that 110 ppm 1,2-dichloropropane is acceptable for a 15-minute exposure period. OSHA feels that nearly all workers may be repeatedly exposed to 1,2-dichloropropane at these levels, day after day, without harmful effects (see Section 1.7). The amount at which the smell of 1,2-dichloropropane is first noticed is 0.25 ppm; therefore, most people would probably smell 1,2-dichloropropane before it reached a harmful level. Continued exposure to the odor may reduce the ability to smell 1,2-dichloropropane at 0.25 ppm. For more information on the amounts of 1,2-dichloropropane that cause effects in humans and animals, see Chapter 2.

1.7 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

The Occupational Safety and Health Administration (OSHA) regulates levels of 1,2-dichloropropane in the workplace. The limit for an 8-hour workday, 40-hour workweek is an average of 75 ppm and the limit for a 15-minute exposure is an average of 110 ppm. The Environmental Protection Agency (EPA) requires a notice when discharges or spills of 1000 pounds or more of 1,2-dichloropropane are made into the environment. For more information on Federal and State recommendations, see Chapter 7.

1.8 WHERE CAN I GET MORE INFORMATION?

If you have further questions or concerns, please contact your State Health or Environmental Department or:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road, E-29
Atlanta, Georgia 30333

2. HEALTH EFFECTS

2.1 INTRODUCTION

This chapter contains descriptions and evaluations of studies and interpretation of data on the health effects associated with exposure to 1,2-dichloropropane. Its purpose is to present levels of significant exposure for 1,2-dichloropropane based on toxicological studies, epidemiological investigations, and environmental exposure data. This information is presented to provide public health officials, physicians, toxicologists, and other interested individuals and groups with (1) an overall perspective of the toxicology of 1,2-dichloropropane and (2) a depiction of significant exposure levels associated with various adverse health effects.

2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE

To help public health professionals address the needs of persons living or working near hazardous waste sites, the data in this section are organized first by route of exposure -- inhalation, oral, and dermal -- and then by health effect -- death, systemic, immunological, neurological, developmental, reproductive, genotoxic, and carcinogenic effects. These data are discussed in terms of three exposure periods -- acute, intermediate, and chronic.

Levels of significant exposure for each exposure route and duration (for which data exist) are presented in tables and illustrated in figures. The points in the figures showing no-observed-adverse-effect levels (NOAELS) or lowest-observed-adverse-effect levels (LOAELs) reflect the actual doses (levels of exposure) used in the studies. LOAELs have been classified into "less serious" or "serious" effects. These distinctions are intended to help the users of the document identify the levels of exposure at which adverse health effects start to appear, determine whether or not the intensity of the effects varies with dose and/or duration, and place into perspective the possible significance of these effects to human health.

The significance of the exposure levels shown on the tables and graphs may differ depending on the user's perspective. For example, physicians concerned with the interpretation of clinical findings in exposed persons or with the identification of persons with the potential to develop such disease may be interested in levels of exposure associated with "serious effects." Public health officials and project managers concerned with response actions at Superfund sites may want information on levels of exposure associated with more subtle effects in humans or animals (LOAEL) or exposure levels below which no adverse effects (NOAEL) have been observed. Estimates of levels posing minimal risk to humans (minimal risk levels, MRLs) are of interest to health professionals and citizens alike.

2. HEALTH EFFECTS

For certain chemicals, levels of exposure associated with carcinogenic effects may be indicated in the figures. These levels reflect the actual doses associated with the tumor incidences reported in the studies cited. Because cancer effects could occur at lower exposure levels, the figures also show estimated excess risks, ranging from a risk of one in 10,000 to one in 10,000,000 ($10m^4$ to $10m^7$), as developed by EPA.

Estimates of exposure levels posing minimal risk to humans (MRLs) have been made, where data were believed reliable, for the most sensitive noncancer end point for each exposure duration. MRLs include adjustments to reflect human variability and, where appropriate, the uncertainty of extrapolating from laboratory animal data to humans. Although methods have been established to derive these levels (Barnes et al. 1987; EPA 1980), uncertainties are associated with the techniques.

2.2.1 Inhalation Exposure

2.2.1.1 Death

No studies were located regarding lethal effects in humans following inhalation exposure to 1,2-dichloropropane.

The lethality after a single exposure by inhalation to 1,2-dichloropropane has been determined in rats and mice. Smyth et al. (1969) and Pozzani et al. (1959) reported LC50 values of 2000 ppm and 3029 ppm, respectively, after a single n-hour exposure in rats. Carpenter et al. (1949) determined that 2000 ppm resulted in the death of 2/6, 3/6 or 4/6 rats after a single 4-hour exposure to 1,2-dichloropropane; Heppel et al. (1946) reported the death of 3/12 rats after a single 7-hour exposure of 1600 ppm; Highman and Heppel (1946) reported the death of 6/24 rats several hours after one 7-hour exposure to 2200 ppm; and Nitschke and Johnson (1983) found no mortality in rats exposed to 1000 ppm 1,2-dichloropropane for 6 hours. Dow Chemical (1982) reported an LC_{50} value of 480 ppm in mice after a single 10-hour exposure to 1,2-dichloropropane. All mice (22-26 animals) died after a single exposure of four hours to 1000 ppm or 1500 ppm, while 3/10 mice died after a single two-hour exposure to 1500 ppm. Nitschke and Johnson (1983) reported the death of all mice within 24 hours of a 6-hour exposure to 1500 ppm 1,2-dichloropropane and, following a 6-hour exposure to 500 mm, mice became lethargic and 2/5 mice died within 3 days of exposure. The concentration of 480 ppm in air from the Dow Chemical (1982) study is presented in Table l-2.

Lethality was observed in rats, mice, guinea pigs and rabbits repeatedly exposed by inhalation to 1,2-dichloropropane for 14 days or less (acute exposure is defined as treatment for ≤14 calendar days). Exposures of 7 hours/day, 5 days/week for 2-10 exposures in the Heppel et al. (1946) study resulted in the deaths of 8/39 rats exposed to 1000 ppm; 3/18 rats and 3/18 guinea pigs exposed to 1500 ppm; and 8/20 rats, 11/16 guinea pigs and 2/4 rabbits exposed to 2200 ppm. Five consecutive days of -/-hour exposures

of 1600 ppm resulted in the death of 0/13 rats, 0/10 guinea pigs and l/2 rabbits (Heppel et al. 1946). Highman and Heppel (1946) reported the death of 7/20 guinea pigs after 2-3 exposures of 7 hours to 2200 ppm 1,2-dichloropropane. Heppel et al. (1948) observed no lethality in rats or guinea pigs following l-9, -7-hour exposures to 400 ppm 1,2-dichloropropane. Nitschke and Johnson (1983) reported no compound-related mortality in rats and rabbits intermittently exposed for 2 weeks to ≤1000 ppm or in mice exposed to ≤300 ppm 1,2-dichloropropane (6 hours/day, 4 to 5 days/week). The concentrations of 1000 ppm in air for rats and 1500 ppm in air for guinea pigs (Heppel et al. 1946) are presented in Table l-2.

The lethality of 1,2-dichloropropane inhaled repeatedly over an intermediate time period (intermediate exposure is defined as treatment for 15 to 364 calendar days) was reported for rats, mice, guinea pigs, rabbits and dogs. Exposures of 7 hours/day, 5 days/week for 11 to 128 exposures in the Heppel et al. (1946) study resulted in the death of 17/45 rats, 3/12 guinea pigs, 0/4 rabbits and 4/8 dogs exposed to 1000 ppm; and 4/18 rats, 2/18 guinea pigs and l/4 rabbits exposed to 1500 ppm. Heppel et al. (1948) observed no lethality in rats, dogs and guinea pigs exposed to 12-140, 7-hour exposures to 400 ppm 1,2-dichloropropane. Nitschke et al. (1988) reported no compound-related mortality in rats and mice intermittently exposed for 13 weeks to ≤150 ppm or in rabbits exposed to <1000 ppm 1,2-dichloropropane (6 hours/day, 5 days/week). Heppel et al. (1948) determined that 37 exposures of 4-7 hours at 400 ppm resulted in the death of 77/80 mice. The cause of death was not given, but some of the mice that died after receiving 14-28 exposures showed moderate to marked congestion and fatty degeneration of the liver, extensive centrolobular coagulation necrosis of the liver, and slight to moderate fatty degeneration of the kidney. The concentrations of 400 ppm in air for mice (Heppel et al. 1948) and 1000 ppm in air for rats, guinea pigs and dogs (Heppel et al. 1946) are presented in Table l-2.

No studies were found which determined the toxicity of 1,2-dichloropropane after inhalation for a chronic period of time (chronic exposure is defined as treatment for ≥365 calendar days).

The highest reliable NOAEL value and all reliable LOAEL values for lethal effects in each species and duration category are reported in Table 2-l and plotted in Figure 2-l. The Carpenter et al. (1949) study cannot be used as the basis for a LOAEL in rats since a small number of animals were evaluated (six), and it is not clear if controls were used. The data evaluating the lethal effects of 1,2-dichloropropane on rabbits in the Heppel et al. (1946) study and on rats and mice in the Nitschke and Johnson (1983) study cannot be used as a basis for NOAELs and LOAELs since so few animals were used (four rabbits, five mice, five rats).

TABLE 2-1. Levels of Significant Exposure to 1,2-Dichloropropane - Inhalation

Graph Key	Species	Duration/ Frequency Exposure		NOAEL[b] (ppm)	LOAEL[a] (Effect)		Reference
					Less Serious (ppm)	Serious (ppm)	
ACUTE EXPOSURE							
Lethality							
1	rat	7 hr				2200 (death)	Highman and Heppel 1946
2	rat	7 hr				1600 (death)	Heppel et al. 1946
3	rat	8 hr				2000 (LC_{50})	Smyth et al. 1969
4	rat	7 hr, 5 d/wk 3-9 exp		400			Heppel et al. 1948
5	rat	7 hr/day, 5 d/wk 6-10 exp				1000 (death)	Heppel et al. 1946
6	mouse	4 hr				1000 (death)	Heppel et al. 1946
7	mouse	6 hr				500 (2/5 died)	Nitschke and Johnson 1983
8	mouse	10 hr				480 (LC_{50})	Dow Chem. 1982
9	mouse	2 wk 4-5 d/wk 6 hr/d		300			Nitschke and Johnson 1983
10	gn pig	4 hr, 7 hr 2-3 exp				2200 (death)	Highman and Heppel 1946
11	gn pig	7 hr, 5 d/wk 6 exp				1500 (death)	Heppel et al. 1946
12	gn pig	7 hr 1-4 exp		400			Heppel et al. 1948
13	rabbit	2 wk 4-5 d/wk 6 hr/d		1000			Nitschke and Johnson 1983
14	rat	6 hr	Hepatic	1500			Nitschke and Johnson 1983
15			Renal	1500			

TABLE 2-1 (continued)

Graph Key	Species	Duration/ Frequency Exposure		NOAEL[b] (ppm)	LOAEL[a] (Effect)		Reference
					Less Serious (ppm)	Serious (ppm)	
Systemic							
16	rat	4 hr, 7 hr	Hepatic		2200 (increased fat)		Highman and Heppel 1946
17		1-5 exp	Renal		2200 (increased fat)		
18	rat	2 wk 4-5 d/wk	Resp		100[c] (nasal mucosa degeneration)		Nitschke and Johnson 1983
19		6 hr/d	Hemato	1000			
20	mouse	6 hr	Hepatic			500 (hemorrhagic necrosis)	Nitschke and Johnson 1983
21			Renal	1500			
22, 23	mouse	2 wk 4-5 d/wk	Resp	30	100 (nasal mucosa degeneration)		Nitschke and Johnson 1983
24		6 hr/d	Hemato	300			
25, 26			Hepatic	100	300 (vacuolization increased liver weight)		
27	gn pig	7 hr 1-8 exp	Ocular			2200 (conjuntivitis)	Heppel et al. 1946
28	gn pig	7 hr	Hepatic	400			Heppel et al. 1948
29		1-4 exp	Renal	400			
30	gn pig	4 hr, 7 hr	Hepatic		2200 (increased fat)		Highman and Heppel 1946
31		1-5 exp	Renal		2200 (increased fat)		
32, 33	rabbit	2 wk 4-5 d/wk	Resp	300	1000 (nasal mucosa degeneration)		Nitschke and Johnson 1983
34		6 hr/d	Hemato	1000			
35			Hepatic	1000			
36			Renal	1000			
Immunological							
37	rat	2 wk 4-5 d/wk 6 hr/d		1000			Nitschke and Johnson 1983

TABLE 2-1 (continued)

Graph Key	Species	Duration/ Frequency Exposure	NOAEL[b] (ppm)	LOAEL[a] (Effect)		Reference
				Less Serious (ppm)	Serious (ppm)	
Immunological						
38, 39	mouse	2 wk 4-5 d/wk 6 hr/d	100	300 (decreased weight of thymus, decreased lymphoid cells)		Nitschke and Johnson 1983
Neurological						
40, 41	rat	6 hr	500		1500 (anesthesia)	Nitschke and Johnson 1983
42	mouse	6 hr			500 (lethargy and death)	Nitschke and Johnson 1983
Reproductive						
43	rat	2 wk 4-5 d/wk 6 hr/d	1000			Nitschke and Johnson 1983
44	mouse	2 wk 4-5 d/wk 6 hr/d	300			Nitschke and Johnson 1983
45	rabbit	2 wk 4-5 d/wk 6 hr/d	1000			Nitschke and Johnson 1983
INTERMEDIATE EXPOSURE						
Lethality						
46	rat	7 hr/d 5 d/wk 12-59 exp			1000 (death)	Heppel et al. 1946
47	rat	7 hr, 5 d/wk 12-140 exp	400			Heppel et al. 1948
48	mouse	4-7 hr 15-37 exp			400 (death)	Heppel et al. 1948

TABLE 2-1 (continued)

Graph Key	Species	Duration/ Frequency Exposure		NOAEL[b] (ppm)	LOAEL[a] (Effect) Less Serious (ppm)	LOAEL[a] (Effect) Serious (ppm)	Reference
Lethality							
49	mouse	13 wk 5 d/wk 6 hr/d		150			Nitschke et al. 1988
50	gn pig	7 hr, 5 d/wk 134 exp		400			Heppel et al. 1948
51	gn pig	7 hr, 5 d/wk 22-126 exp				1000 (death)	Heppel et al. 1946
52	rabbit	13 wk 5 d/wk 6 hr/d		1000			Nitschke et al. 1988
53	dog	7 hr, 5 d/wk 27-96 exp				1000 (death)	Heppel et al. 1946
54	dog	7 hr, 5 d/wk 134 exp		400			Heppel et al. 1948
Systemic							
55	rat	13 wk 5 d/wk	Resp		15[d] (upper respiratory lesions)		Nitschke et al. 1988
56		6 hr/d	Cardio	150			
57			Gastro	150			
58			Hemato	150			
59			Musc/skel	150			
60			Derm/Oc	150			
61, 62			Body Weight	50	150 (decreased body weight gain)		
63	rat	7 hr/d	Hepatic	1000			Heppel et al. 1946
64		5 d/wk 12-59 exp	Renal	1000			

TABLE 2-1 (continued)

Graph Key	Species	Duration/ Frequency Exposure		NOAEL[b] (ppm)	LOAEL[a] (Effect) Less Serious (ppm)	LOAEL[a] (Effect) Serious (ppm)	Reference
Systemic							
65	mouse	13 wk	Resp	150			Nitschke et al. 1988
66		5 d/wk	Cardio	150			
67		6 hr/d	Gastro	150			
68			Hemato	150			
69			Musc/skel	150			
70			Hepatic	150			
71			Renal	150			
72			Derm/Oc	150			
73			Body Weight	150			
74	gn pig	7 hr	Hepatic	1500			Heppel et al. 1946
75		5 d/wk 11 exp	Renal	1500			
76	rabbit	13 wk 5 d/wk	Resp		1000 (olfactory degeneration)		Nitschke et al. 1988
77		6 hr/d	Cardio	1000			
78			Gastro	1000			
79			Hemato		150 (anemia)		
80			Musc/skel	1000			
81			Hepatic	1000			
82			Renal	1000			
83			Derm/Oc	1000			
84			Body Weight	1000			
85	dog	7 hr	Hepatic	400			Heppel et al. 1948
86		5 d/wk 134 exp	Renal	400			
Immunological							
87	rat	13 wk 5 d/wk 6 hr/d		150			Nitschke et al. 1988
88	mouse	13 wk 5 d/wk 6 hr/d		150			Nitschke et al. 1988

TABLE 2-1 (continued)

Graph Key	Species	Duration/ Frequency Exposure	NOAEL[b] (ppm)	LOAEL[a] (Effect)		Reference
				Less Serious (ppm)	Serious (ppm)	
Immunological						
89	rabbit	13 wk 5 d/wk 6 hr/d	1000			Nitschke et al. 1988
Neurological						
90	rat	13 wk 5 d/wk 6 hr/d	150			Nitschke et al. 1988
91	mouse	13 wk 5 d/wk 6 hr/d	150			Nitschke et al. 1988
92	rabbit	13 wk 5 d/wk 6 hr/d	1000			Nitschke et al. 1988
Reproductive						
93	rat	13 wk 5 d/wk 6 hr/d	150			Nitschke et al.1988
94	mouse	13 wk 5 d/wk 6 hr/d	150			Nitschke et al. 1888
95	rabbit	13 wk 5 d/wk 6 hr/d	1000			Nitschke et al. 1988

[a]LOAEL - Lowest Observed Adverse Effect Level
[b]NOAEL - No Observed Adverse Effect Level
[c]Used to derive acute inhalation MRL; dose adjusted for intermittent exposure, and divided by an uncertainty factor of 1000 (10 for use of a LOAEL, 10 for extrapolation from animals to humans and 10 for human variability), resulting in an MRL of 50 ppb (0.050 ppm).
[d]Used to derive intermediate inhalation MRL; dose adjusted for intermittent exposure, and divided by an uncertainty factor of 1000 (10 for use of a LOAEL, 10 for extrapolation from animals to humans and 10 for human variability), resulting in an MRL of 7 ppb (0.007 ppm).

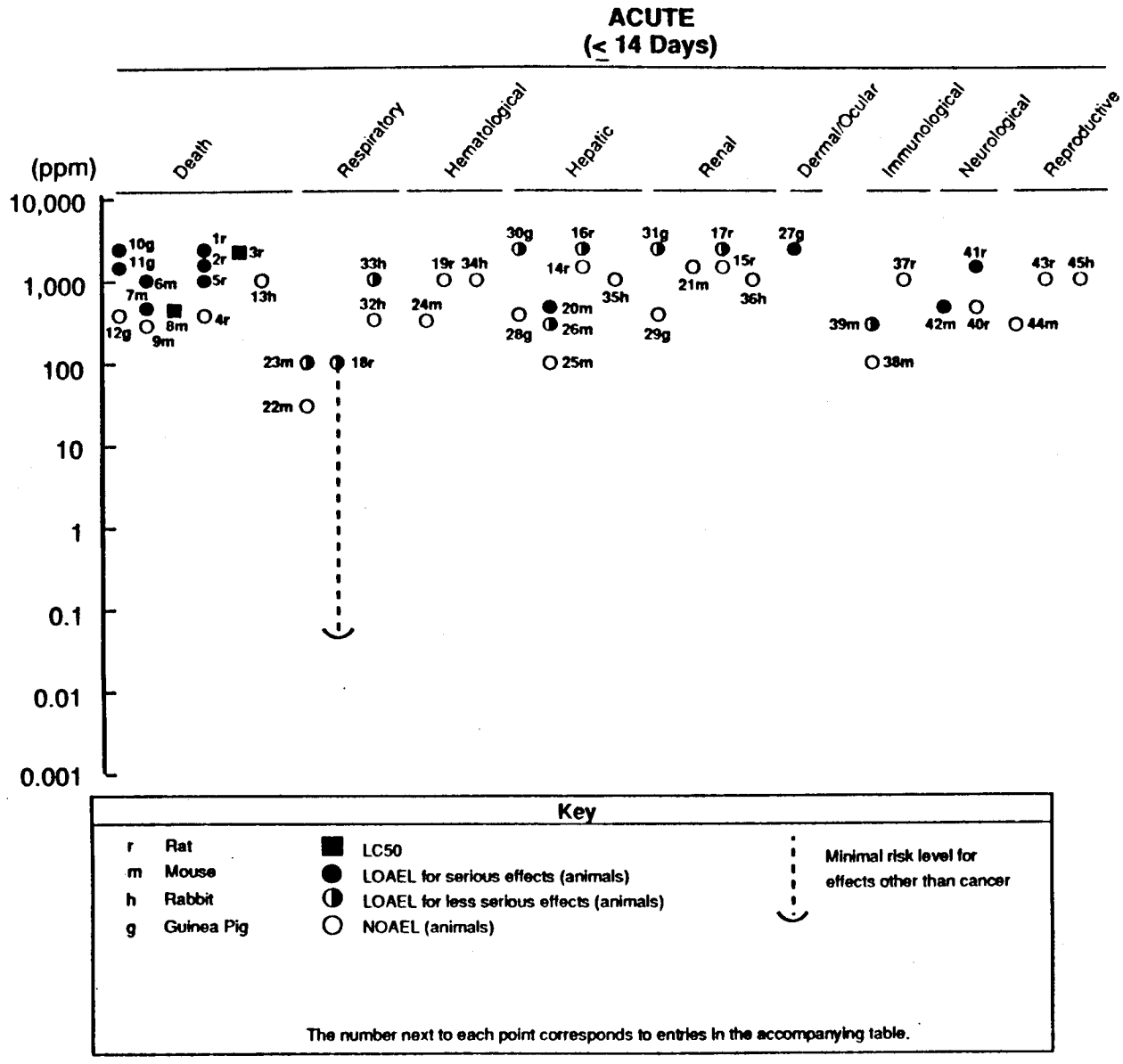


FIGURE 2-1. Levels of Significant Exposure to 1,2 - Dichloropropane - Inhalation

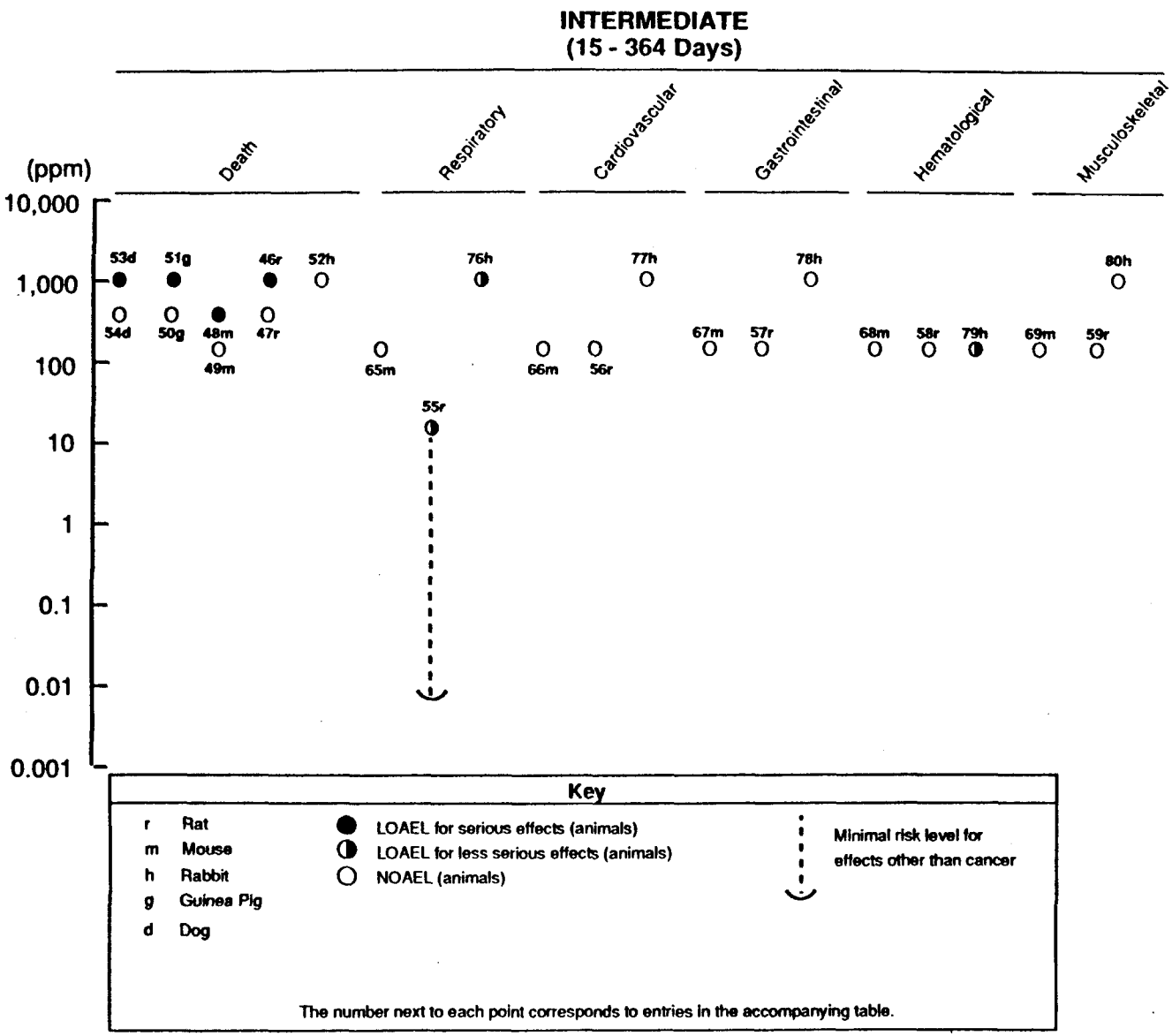


FIGURE 2-1. Levels of Significant Exposure to 1,2 - Dichloropropane - Inhalation (Continued)

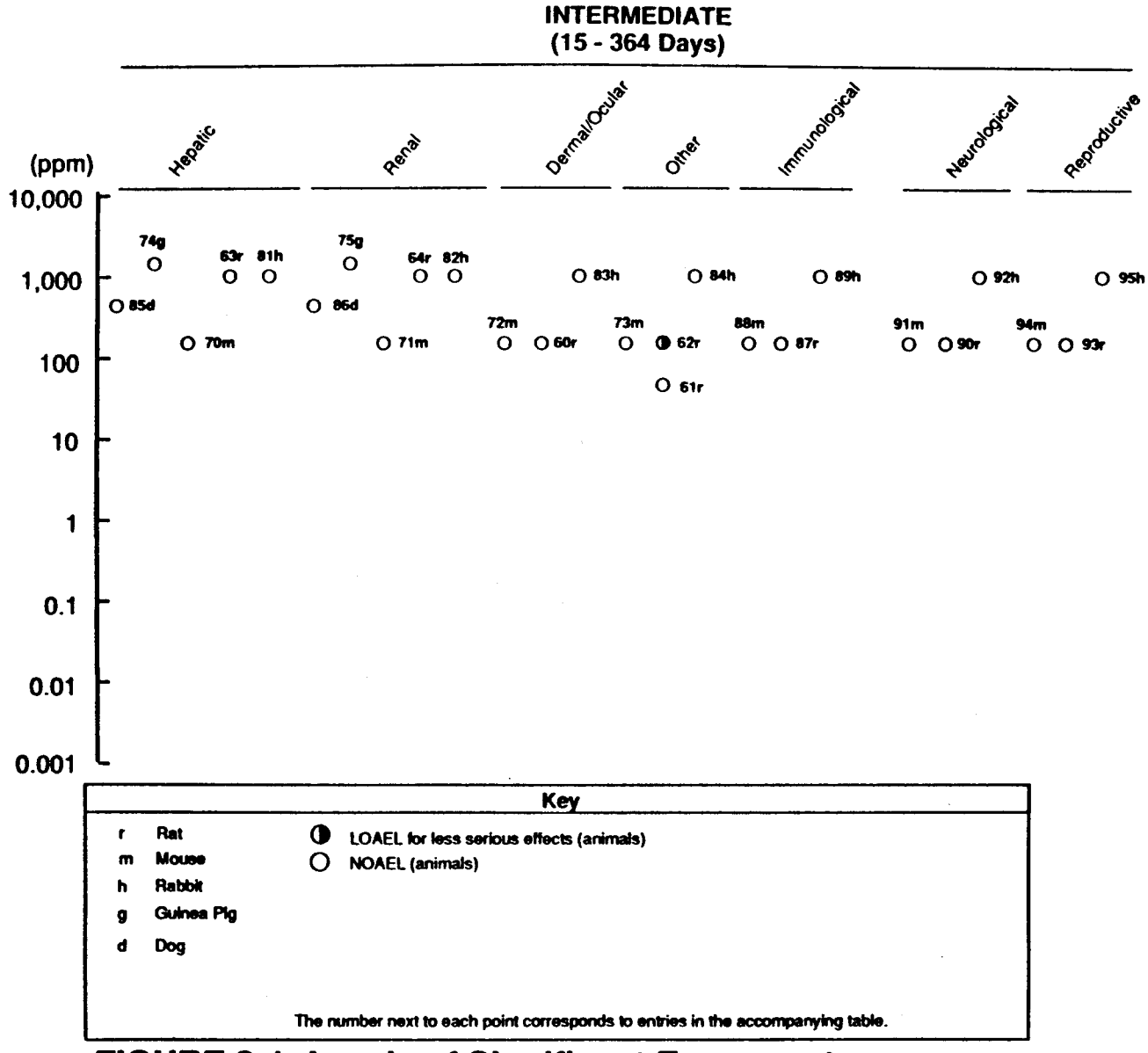


FIGURE 2-1. Levels of Significant Exposure to 1,2 - Dichloropropane - Inhalation (Continued)

2.2.1.2 Systemic Effects

Respiratory Effects. Rubin (1988) described the health effects in humans resulting from exposure to an accidental spill of 2000 gallons of 1,2-dichloropropane. The exposure resulted in chest discomfort, dyspnea, and a cough in some of the patients, indicating that 1,2-dichloropropane is a respiratory tract irritant. Air concentrations of 1,2-dichloropropane were not measured or estimated.

The effects of 1,2-dichloropropane on the respiratory systems of animals acutely exposed (1-14 days) were determined for rats, mice, and rabbits, Degeneration of the nasal mucosa was found in rats and mice exposed to ≥100 ppm and in rabbits exposed to 1000 ppm 1,2-dichloropropane for 2 weeks (6 hours/day, 4 to 5 days/week) (Nitschke and Johnson 1983). In the rats, the severity of the nasal mucosa degeneration was concentration related and the effects occurred at the lowest exposure level. In the mice, no adverse respiratory effects were found at an exposure level of 30 ppm and the effects found at 100 ppm were less severe than those found in the rat. In the rabbits, no adverse respiratory effects were found at an exposure level of 300 ppm. Therefore, rats appear to be the most sensitive species to the respiratory effects of 1,2-dichloropropane exposure. The concentrations of 100 ppm in air for rats and mice and of 1000 ppm in air for rabbits (Nitschke and Johnson 1983) are presented in Table l-2.

The effects of 1,2-dichloropropane on the respiratory systems of animals exposed for an intermediate time period (15-364 days) were determined for rats, mice and rabbits. Rabbits exposed to 1000 ppm and rats exposed to ≥50 ppm had slight degeneration of the olfactory epithelium; rats exposed to ≥15 ppm also had slight degeneration of the respiratory epithelium (Nitschke et al. 1988). No adverse effects on the respiratory system were found in rabbits exposed to ≤500 ppm or in mice exposed to ≤150 ppm (Nitschke et al. 1988). The concentration of 15 ppm in air (Nitschke et al. 1988) is presented in Table 1-2.

The highest reliable NOAEL value and all reliable LOAEL values for respiratory effects in each species and duration category are reported in Table 2-1 and plotted in Figure 2-1. Both the acute study of Nitschke and Johnson (1983) and the intermediate study of Nitschke et al. (1988) determined that rats are the most sensitive species to the respiratory effects of 1,2-dichloropropane. Therefore, the LOAEL of 100 ppm for respiratory effects in rats in the acute study (Nitschke and Johnson 1983) and the LOAEL of 15 ppm for respiratory effects in rats in the intermediate study (Nitschke et al. 1988) will be used as the basis for the acute and intermediate MRL, respectively. Based on the LOAEL of 100 ppm (Nitschke and Johnson 1983), an acute MRL of 50 ppb (0.05 ppm) was calculated and based on the LOAEL of 15 ppm (Nitschke et al. 1988), an intermediate MRL of 7 ppb (0.007 ppm) was calculated. These calculations are described in the footnote in Table 2-l.

2. HEALTH EFFECTS

Cardiovascular Effects. No studies were located regarding cardiovascular effects in humans following inhalation exposure to 1,2-dichloropropane.

No adverse effects of 1,2-dichloropropane on the cardiovascular system were found following histological examination of the heart and aorta of rats and mice exposed to ≤150 ppm and of rabbits exposed to ≤1000 ppm, 6 hours/day, 5 days/week for 13 weeks (Nitschke et al. 1988). These NOAEL values for rats, mice and rabbits are reported on Table 2-l and plotted on Figure 2-1.

Heppel et al. (1946) observed fatty degeneration of the heart in dogs that were exposed to 1000 ppm 1,2-dichloropropane for 7 hours/day, 5 days/week for 27-128 exposures. This effect occurred only in animals that died (the dogs died after 27-96 exposures); therefore, it is inappropriate to consider this concentration a LOAEL for cardiovascular effects in dogs.

Gastrointestinal Effects. Pozzi et al. (1985) reported vomiting and abdominal pain in a young woman who had been sniffing a stain remover, consisting primarily (98%) of 1,2-dichloropropane, to alleviate nervousness, but no dose was determined. The woman sniffed the chemical four times in one night and the symptoms appeared the next morning. ,The woman recovered completely after 3 weeks of hospitalization.

No adverse effects of 1,2-dichloropropane on the gastrointestinal system were found following histological examination of the stomach, large intestine, and small intestine of rats and mice exposed to ≤150 ppm and of rabbits exposed to ≤1000 ppm, 6 hours/day, 5 days/week for 13 weeks (Nitschke et al. 1988). These NOAEL values for rats, mice, and rabbits are reported on Table 2-l and plotted on Figure 2-l.

Hematological Effects. Pozzi et al. (1985) discussed two case studies in which 1,2-dichloropropane, at unreported concentrations, was inhaled over a short period of time. One case involved the inhalation of 1,2-dichloropropane over the course of one evening, and the second case involved the inhalation over 6 hours while a woman was using a solvent containing 1,2-dichloropropane to. clean. Effects of exposure included epistaxis (nosebleed), hemolytic anemia and disseminated intravascular coagulation (DIC). Both patients recovered.

No hematological effects were observed in rats that were acutely exposed to 433 ppm 1,2-dichloropropane (Sidorenko et al. 1979).

Hematological effects as a result of exposure to 1,2-dichloropropane for intermediate durations have been evaluated in rabbits, mice, and rats. No hematological effects were observed in rats or mice exposed to ≤150 ppm (Nitschke et al. 1988). A dose-related increased severity of anemia

occurred in rabbits exposed to ≥150 ppm (Nitschke et al. 1988). The concentration of 150 ppm in air (Nitschke et al. 1988) is presented in Table 1-2.

The highest reliable NOAEL value and all reliable LOAEL values for hematological effects in each species and duration category are reported in Table 2-l and plotted in Figure 2-l. The Sidorenko et al. (1979) study cannot be considered a reliable study since the number of animals used was not reported.

Musculoskeletal Effects. No studies were located regarding musculoskeletal effects in humans following inhalation exposure to 1,2-dichloropropane.

No adverse effects of 1,2-dichloropropane on the musculoskeletal system were found following histological examination of the bone of rats and mice exposed to ≤150 ppm and of rabbits exposed to ≤1000 ppm, 6 hours/day, 5 days/week for 13 weeks (Nitschke et al. 1988). These NOAEL values for rats, mice, and rabbits are reported on Table 2-l and plotted on Figure 2-l.

Hepatic Effects. The liver is one of the main target organs for the toxic effects of 1,2-dichloropropane. Pozzi et al. (1985) discussed two human case studies where 1,2-dichloropropane was inhaled, leading to hepatic failure in one case and hepatic damage in the other. In the first case, a 55-year-old woman was already suffering from membrano-proliferative glomerulonephritis and undergoing home dialysis 3 times a week. The patient was hospitalized with abdominal pain after inhaling cleaning solution which contained 60% 1,2-dichloropropane for 6 hours; the remaining 40% of the solution was a mixture of acetone, isobutyl alcohol, and n-butyl acetate. Laboratory tests (aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), prothrombin) showed severe hepatic failure but the woman recovered after a week of hospitalization. In the second case, a 20-year-old woman deliberately inhaled Trielina (98% 1,2-dichloropropane), over the course of one evening, as a means of sedation and was admitted to the hospital. Laboratory tests (AST, ALT, total bilirubin, prothrombin) showed acute liver damage. The woman recovered after 3 weeks of hospitalization. Concentrations were not reported for these chemical exposures so that a LOAEL cannot be determined.

Hepatic effects of acute inhalation exposure to 1,2-dichloropropane were evaluated in guinea pigs, mice, rabbits, and rats. Fatty degeneration of the liver occurred in guinea pigs and rats acutely exposed to 2200 ppm (Heppel et al. 1946; Highman and Heppel 1946); adverse effects were not observed in guinea pigs and rats acutely exposed to 400 ppm (Heppel et al. 1948) or in rats exposed to 1000 ppm (Heppel et al. 1946). Drew et al. (1978) found no alterations of serum levels of liver enzymes, which would indicate liver damage, in rats that were exposed to 1000 ppm for 4 hours. Nitschke and Johnson (1983) found no histopathologic effects on the liver in rats treated with a single 6-hour exposure of 1500 ppm 1,2-dichloropropane

or in rats and rabbits exposed to 1000 ppm for 2 weeks (6 hours/day, 4-5 days/week). In mice, extensive hemorrhagic necrosis was found in animals exposed for 6 hours to 500 ppm 1,2-dichloropropane. Following intermittent exposure to 300 ppm for 2 weeks (6 hours/day, 4-5 days/week), increased liver weight and hepatocellular hypertrophy were observed in mice (Nitschke and Johnson 1983).

The hepatic effects of the inhalation of 1,2-dichloropropane administered for intermediate time periods were studied in rats, mice, rabbits, guinea pigs, and dogs. Adverse effects on the liver were not observed in dogs, rats and guinea pigs exposed to 400 ppm (Heppel et al. 1948); in rats, guinea pigs, rabbits or dogs exposed to 1000 ppm; and in guinea pigs and rabbits exposed to 1500 ppm (Heppel et al. 1946). Nitschke et al. (1988) observed no histopathologic effects on the liver in rats or mice exposed to ≤150 ppm or in rabbits exposed to ≤1000 ppm 1,2-dichloropropane 6 hours/day, 5 days/week for 13 weeks.

The highest reliable NOAEL value and all reliable LOAEL values for hepatic effects in each species and duration category are reported in Table 2-l and plotted in Figure 2-l. The data regarding hepatic effects in rabbits in the Heppel et al. (1946) study are not reliable since a small number of animals (3-4) was used for evaluation.

Renal Effects. Pozzi et al. (1985) reported a case study of a 20-year-old female who deliberately inhaled an unknown amount of Trielina (98% 1,2-dichloropropane) over the course of one evening. Laboratory tests (serum creatine, blood urea nitrogen (BUN)) showed severe renal failure. Scant urine output (oliguria) and blood in the urine (hematuria) were also seen. Renal biopsy findings showed acute tubular necrosis. Other systems, such as the liver, were similarly effected. The woman recovered after 3 weeks of hospitalization.

Renal effects as a result of acute inhalation exposure to 1,2-dichloropropane were evaluated in rats, mice, and guinea pigs. Fatty degeneration of the kidney occurred in rats and guinea pigs acutely exposed to 2200 ppm (Highman and Heppel 1946); adverse effects were not observed in rats and guinea pigs acutely exposed to 400 ppm (Heppel et al. 1948) or in rats exposed to 1000 ppm (Heppel et al. 1946). The renal effects observed after acute exposure in rats and guinea pigs are similar to the effects seen in the liver (Highman and Heppel 1946). No adverse effects on the kidneys were found following histopathologic examination in rats and mice exposed for 6 hours to 1500 ppm 1,2-dichloropropane or in rats and rabbits exposed to 1000 ppm and in mice exposed to 300 ppm for 2 weeks (6 ,hours/day, 4-5 days/week) (Nitschke and Johnson 1983).

Renal effects for intermediate inhalation exposure to 1,2-dichloropropane were evaluated in rats, guinea pigs, rabbits, and dogs. Adverse effects on the kidney were not observed in dogs, guinea pigs and rats exposed to 400 ppm (Heppel et al. 1948), in guinea pigs, rats, rabbits

and dogs exposed to 1000 ppm, and in guinea pigs and rabbits exposed to 1500 ppm (Heppel et al. 1946). Nitschke et al. (1988) observed no histopathologic effects on the kidneys in rats and mice exposed to ≤150 ppm and in rabbits exposed to ≤1000 ppm 1,2-dichloropropane for 13 weeks (6 hours/day, 5 days/week).

The highest reliable NOAEL value and all reliable LOAEL values for renal effects in each species and duration category are reported in Table 2-l and plotted in Figure 2-1. The data regarding renal effects in rabbits in the Heppel et al. (1946) study are not reliable since a small number of animals (3-4) were used for evaluation.

Dermal/Ocular Effects. Periorbital and conjunctival hemorrhages were seen in a patient that was admitted to a hospital after exposure to vapors of 1,2-dichloropropane (Pozzi et al. 1985). It was not clear if the hemorrhages resulted from inhalation of 1,2-dichloropropane or from direct exposure of the eye to the 1,2-dichloropropane vapor. No concentration information was provided.

Severe conjunctivitis occurred in guinea pigs acutely exposed to 2200 ppm of 1,2-dichloropropane vapor (Heppel et al. 1946). This concentration of 1,2-dichloropropane also produced death; 5 exposures of 7 hours each resulted in the deaths of 11/16 of the animals. The paper did not clearly state at what point, during the 5 exposures, the conjunctivitis was first observed. This concentration represents a LOAEL for ocular effects and is reported in Table 2-l and plotted on Figure 2-l.

No adverse effects on the eye were found following gross and histopathologic examination of the eyes of rats and mice exposed to ≤150 ppm and in rabbits exposed to ≤1000 ppm 1,2-dichloropropane for 13 weeks (6 hours/day, 5 days/week) (Nitschke et al. 1988). These NOAEL values are reported in Table 2-l and plotted on Figure 2-l.

2.2.1.3 Immunological Effects

No studies were located regarding immunological effects in humans following inhalation exposure to 1,2-dichloropropane.

Histologic examination of the bone marrow and thymus revealed no adverse effects on the organs of the immune system in rats and rabbits exposed to 1000 ppm of 1,2-dichloropropane 6 hours/day, 4-5 days/week for 2 weeks (Nitschke and Johnson 1983). In mice exposed to 300 ppm 1,2-dichloropropane for 2 weeks (6 hours/day, 4-5 days/week), a decrease in the absolute and relative thymus weight and a decrease in cortical lymphoid cells were observed (Nitschke and Johnson 1983). Following 13 weeks of exposure to 1,2-dichloropropane (6 hours/day, 5 days/week), no histopathologic effects on the organs of the immune system (bone marrow, thymus) were found in rats (150 ppm), mice (150 ppm), or rabbits (1000 ppm)

(Nitschke et al. 1988). Parameters of immunological function, however, were not assessed in either study so that NOAELs or LOAELs cannot be defined.

2.2.1.4 Neurological Effects

Rubin (1988) described health effects in people who were exposed to unknown concentrations of 1,2-dichloropropane from a tank truck that leaked 2000 gallons of the chemical. Fatigue, possibly attributable to CNS depression, was among the symptoms observed in the exposed people.

Anesthesia was observed in rats during exposure to 1500 ppm 1,2-dichloropropane for 6 hours (Nitschke and Johnson 1983). The rats recovered within an hour after exposure, but remained lethargic. All mice exposed to 1500 ppm for 6 hours appeared anesthetized during exposure and died within 24 hours. Mice exposed to 500 ppm did not exhibit neurological effects during the exposure but became lethargic after the exposure period, and 2/5 of the animals died within 3 days.

No adverse effects on the nervous system were found following observation for overt signs of toxicity (tremors, convulsions, salivation, lacrimination, diarrhea, lethargy) or following histopathologic examination of the brain, spinal cord, and peripheral nerve of rats and mice exposed to $\leq$150 ppm and of rabbits exposed to $\leq$1000 ppm 1,2-dichloropropane 6 hours/day, 5 days/week for 13 weeks (Nitschke et al. 1988). No specialized staining methods were used for examination of the tissues of the nervous system.

Sidorenko et al. (1976) described the sequence of signs of intoxication in mice that were acutely exposed by inhalation to 1,2-dichloropropane. General agitation and decreased coordination of movements occurred initially, followed by sluggishness, amyotonia and sporadic clonic spasms, and subsequently by loss of righting reflex. The loss of the righting reflex occurred at the lowest concentration given, 1000 ppm. Sidorenko et al. (1979) evaluated the neurological effects in rats resulting from acute and intermediate duration exposure to 1,2-dichloropropane. A total threshold indicator (TTI) was used to assess the effects on the CNS, but the details of the TTI were not explained in the study. In addition, control data and numbers of treated rats and mice were not reported, Due to these inadequacies, it is inappropriate to identify LOAELs and NOAELs for neurological effects from these studies.

The highest reliable NOAEL value and all reliable LOAEL values for neurological effects in each species and duration category are reported in Table 2-l and plotted in Figure 2-l.

2.2.1.5 Developmental Effects

No studies were located regarding developmental effects in humans or animals following inhalation exposure to 1,2-dichloropropane.

2.2.1.6 Reproductive Effects

Pozzi et al. (1985) reported the case of a woman who was hospitalized with metrorrhagia (bleeding from the uterus between menstrual periods) after acute inhalation of 1,2-dichloropropane. The metrorrhagia was a transient effect. No information regarding concentration was given.

No histological changes in the testes of rats and rabbits exposed to 1000 ppm 1,2-dichloropropane and of mice exposed to 300 ppm 1,2-dichloropropane for 2 weeks (6 hours/day, 4 to 5 days/week) were observed (Nitschke and Johnson 1983).

No histological changes in the epididymis, prostate, or testes of males and in the oviduct, uterus, cervix, ovaries, or mammary glands of females were observed in rats and,mice exposed to ≤150 ppm and in rabbits exposed to ≤1000 ppm 1,2-dichloropropane for 13 weeks (6 hours/day, 5 days/week) (Nitschke et al. 1988).

The NOAEL values for each species and duration of exposure are reported on Table 2-l and plotted on Figure 2-l.

2.2.1.7 Genotoxic Effects

No studies were located regarding genotoxic effects in humans or animals following inhalation exposure to 1,2-dichloropropane.

2.2.1.8 Cancer

No studies were located regarding carcinogenic effects in humans following inhalation exposure to 1,2-dichloropropane.

Heppel et al. (1948) examined the hepatocarcinogenic effects of 1,2-dichloropropane resulting from intermediate inhalation exposure. It was not clear if tissues other than the liver were examined. In the study, hepatomas were seen in 3 out of 80 mice exposed 37 times to 400 ppm for 4-7 hours. High mortality occurred throughout the study; only three mice survived all exposures plus a 7-month observation period. The hepatomas were observed in the three mice that survived. The morphology of the hepatomas was inadequately characterized and the incidence in controls was not reported, therefore, this study was not used as a basis for a Cancer Effect Level (CEL) in mice after intermediate inhalation exposure.

2.2.2 Oral Exposure

2.2.2.1 Death

There are several cases in the literature of lethality in humans resulting from ingestion of 1,2-dichloropropane. The most common method of

oral exposure was the accidental or intentional ingestion of 1,2-dichloropropane in the form of commercial solvents (Pozzi et al. 1985, Larcan et al. 1977, Perbellini et al. 1985, Zedda et al. (n.d.), Chiappino, and Secchi 1968). The quantity ingested cannot be determined accurately because of factors such as immediate vomiting after ingestion and unknown extent of absorption of 1,2-dichloropropane from the gastrointestinal tract. Typically, clinical signs of 1,2-dichloropropane overexposure in these incidences included primary effects on the CNS, liver, and kidney. Effects on the respiratory system, heart, and blood were also described. Specific causes of death included cardiac arrest and septic shock. No data on the lethal effects of 1,2-dichloropropane in humans resulting from repeated oral exposures, including chronic low-level exposure, were located.

The lethal effects of orally-administered 1,2-dichloropropane in animals have been reported by several investigators. Statistically determined oral LD_{50} values of 1942 mg/kg/day (Pozzani et al. 1959) and 2196 mg/kg/day (Smyth et al. 1969) have been determined for rats. An oral LD_{50} of approximately 2000 mg/kg/day in rats is reported in Table 2-2 and plotted in Figure 2-2.

Rats and mice were administered daily doses of 125-2000 mg/kg/day by gavage for 14 days (NTP 1986). All rats given 2000 mg/kg/day orally died but there was no mortality at ≤1000 mg/kg/day. In mice, increased mortality occurred at ≥500 mg/kg/day, but not at ≤250 mg/kg/day. No short-term studies of 1,2-dichloropropane administered in food were located; therefore, the dose level of 500 mg/kg/day in mice and 2000 mg/kg/day in rats, which were administered by gavage in corn oil (NTP 1986), were converted to an equivalent concentration of 3850 ppm in food for mice and 40,000 ppm in food for rats, for presentation in Table l-4.

Bruckner et al. (1989) reported no lethality in rats treated with up to 1000 mg/kg/day 1,2-dichloropropane by gavage in corn oil for 1, 5, or 10 consecutive days. In a 13-week study reported along with the acute study, 50% of the rats treated with 750 mg/kg/day (the highest dose) died within 10 days and the remaining animals in the treatment group were sacrificed. Also, 50% of the animals treated with 500 mg/kg/day died during the course of the 13-week study. The authors did not attempt to explain this apparent discrepancy in the lethal dose so that no NOAEL or LOAEL values for lethality will be defined.

In intermediate duration oral studies conducted by NTP (1986), rats and mice were administered doses in the range of 30-1000 mg/kg/day by gavage on 5 days/week for 13 weeks. Death was observed at the dose of 500 mg/kg/day but there was no mortality at ≤250 mg/kg/day for both rats and mice.

In chronic (103 weeks) gavage studies conducted by the NTP (1986), increased mortality occurred in female rats and female mice that were treated with 250 mg/kg/day (5 days/week). No increase in mortality occurred in rats or mice that were similarly treated with ≤125 mg/kg/day. No

TABLE 2-2. Levels of Significant Exposure to 1,2-Dichloropropane - Oral

Graph Key	Species	(Route)[c]	Duration/ Frequency Exposure		NOAEL[b] (mg/kg/day)	LOAEL[a] (Effect) Less Serious (mg/kg/day)	LOAEL[a] (Effect) Serious (mg/kg/day)	Reference
ACUTE EXPOSURE								
Lethality								
1, 2	rat	(G)	1/d, 14 d		1000		2000 (death)	NTP 1986
3	rat	(G)	one dose				2000 (LD_{50})	Pozzani et al. 1959 Smyth et al.1969
4, 5	mouse	(G)	1/d, 14 d		250		500 (death)	NTP 1986
Systemic								
6	rat	(G)	1, 5, 10 d	Resp	1000			Bruckner et al. 1989
7				Gastro	1000			
8, 9, 10				Hemato	100	250 (mild anemia)	500 (severe anemia)	
11, 12				Hepatic	100	250 (necrosis)		
13, 14				Renal	*500*	*1000 (increased BUN)*		
15, 16				Body Weight	100	250 (decreased body weight gain)		
17	mouse	(G)	14 d	Renal	2000			NTP 1986
18			5 d/wk	Body Weight	2000			
Neurological								
19, 20	rat	(G)	1, 5, 10 d			100[d] (slight CNS depression)	250 (definite CNS depression)	Bruckner et al. 1989
Reproductive								
21, 22	rat	(G)	1, 5, 10 d		250	500 (testicular degeneration)		Bruckner et al. 1989
INTERMEDIATE EXPOSURE								
Lethality								
23, 24	rat	(G)	5 d/wk 13 wk		250		500 (death)	NTP 1986

TABLE 2-2 (continued)

Graph Key	Species	(Route)[c]	Duration/ Frequency Exposure		NOAEL[b] (mg/kg/day)	LOAEL[a] (Effect) Less Serious (mg/kg/day)	LOAEL[a] (Effect) Serious (mg/kg/day)	Reference
25, 26	mouse	(G)	5 d/wk, 13 wk		250		500 (death)	NTP 1986
Systemic								
27, 28	rat	(G)	13 wk 5 d/wk	Hemato		100[e] (slight anemia)	250 (pronounced anemia)	Bruckner et al. 1989
29, 30				Hepatic	250	500 (hyperplosia vacuolization)		
31				Body Weight		100 (decreased body gain)		
32	rat	(G)	5 d/wk	Resp	1000			NTP 1986
33			13 wk	Gastro	1000			
34				Renal	1000			
35				Derm/Oc	1000			
36, 37				Body Weight	250	500 (decreased body weight gain)		
38	mouse	(G)	5 d/wk	Resp	500			NTP 1986
39			13 wk	Gastro	500			
40				Hemato	500			
41				Hepatic	500			
42				Renal	500			
43				Derm/Oc	500			
44				Body Weight	500			
Neurological								
45	rat	(G)	gestation day 6-21			125 (neurotoxic effects)		Kirk et al. 1989
46	rat	(G)	13 wk 5 d/wk				500 (pronounced depression)	Bruckner et al. 1989
Developmental								
47	rat	(G)	gestation day 6-21			125 (delayed ossification)		Kirk et al. 1989

TABLE 2-2 (continued)

Graph Key	Species	(Route)[c]	Duration/ Frequency Exposure		NOAEL[b] (mg/kg/day)	LOAEL[a] (Effect) Less Serious (mg/kg/day)	LOAEL[a] (Effect) Serious (mg/kg/day)	Reference
Reproductive								
48	rat	(G)	gestation day 6-21		125			Kirk et al. 1989
49, 50	rat	(G)	13 wk 5 d/wk		250	500 (testicular degeneration)		Bruckner et al. 1989
CHRONIC EXPOSURE								
Lethality								
51, 52	rat	(G)	5 d/wk 103 wk		125		250 (death)	NTP 1986
53, 54	mouse	(G)	5 d/wk 103 wk		125		250 (death)	NTP 1986
Systemic								
55	rat	(G)	5 d/wk	Resp	250			NTP 1986
56			103 wk	Cardio	250			
57				Gastro	250			
58, 59				Hepatic	125	250 (necrosis)		
60				Renal	250			
61				Derm/Oc	250			
62, 63				Body Weight	62	125 (decreased body weight gain)		
64	mouse	(G)	5 d/wk	Resp	250			NTP 1986
65			103 wk	Cardio	250			
66				Hepatic		125[f] (necrosis)		
67				Renal	250			
68				Derm/Oc	250			
69				Body Weight	250			

TABLE 2-2 (continued)

Graph Key	Species	(Route)[c]	Duration/ Frequency Exposure	NOAEL[b] (mg/kg/day)	LOAEL[a] (Effect)		Reference
					Less Serious (mg/kg/day)	Serious (mg/kg/day)	
Carcinogenic							
70	rat	(G)	5 d/wk 103 wk			250 (mammary tumors)	NTP 1986
71	mouse	(G)	5 d/wk 103 wk			125 (hepatic tumors)	NTP 1986

[a]LOAEL - Lowest Observed Adverse Effect Level
[b]NOAEL - No Observed Adverse Effect Level
[c]Route - G - Gavage
[d]Used to derive acute oral MRL; dose divided by an uncertainty factor of 1000 (10 for use of a LOAEL, 10 for extrapolation from animals to humans, and 10 for human variability), resulting in an MRL of 0.1 mg/kg/day.
[e]Used to derive intermediate oral MRL; dose adjusted for intermittent exposure and divided by an uncertainty factor of 1000 (10 for use of a LOAEL, 10 for extrapolation from animals to humans, and 10 for human variability), resulting in an MRL of 0.07 mg/kg/day.
[f]Used to derive chronic oral MRL; dose adjusted for intermittent exposure and divided by an uncertainty factor of 1000 (10 for use of a LOAEL, 10 for extrapolation from animals to humans, and 10 for human variability), resulting in an MRL of 0.09 mg/kg/day.

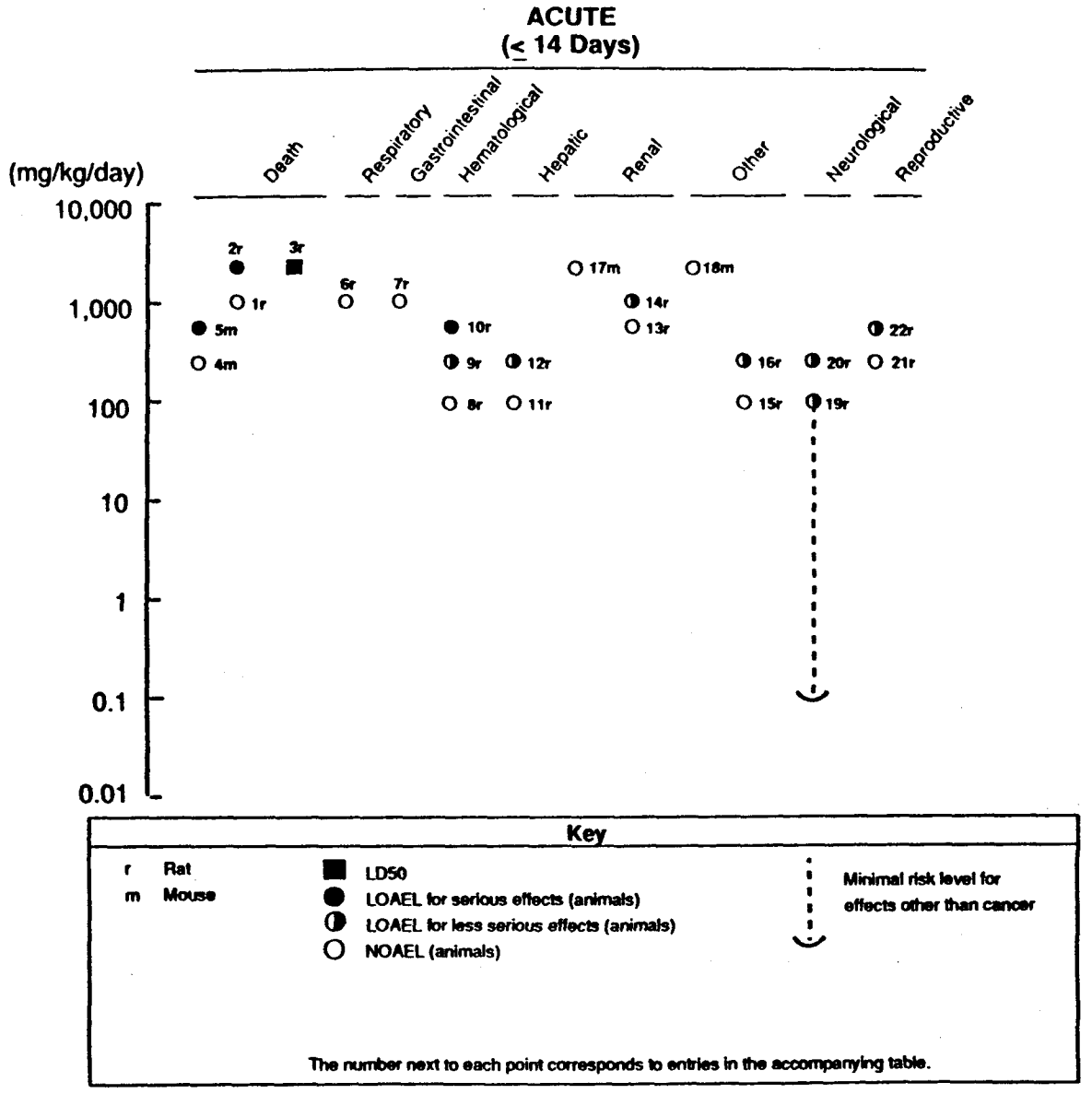


FIGURE 2-2. Levels of Significant Exposure to 1,2 - Dichloropropane - Oral

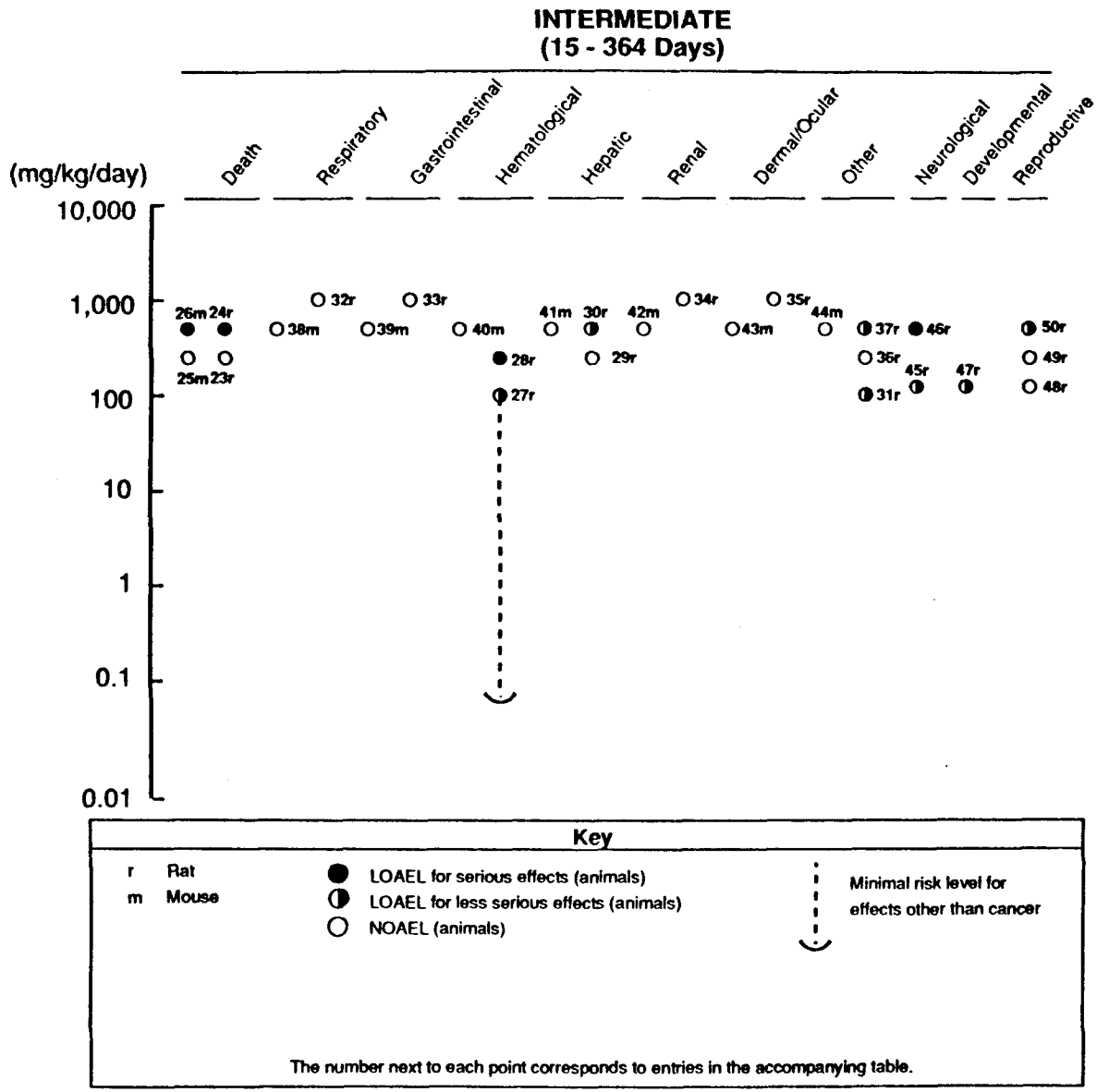


FIGURE 2-2. Levels of Significant Exposure to 1,2 - Dichloropropane - Oral (Continued)

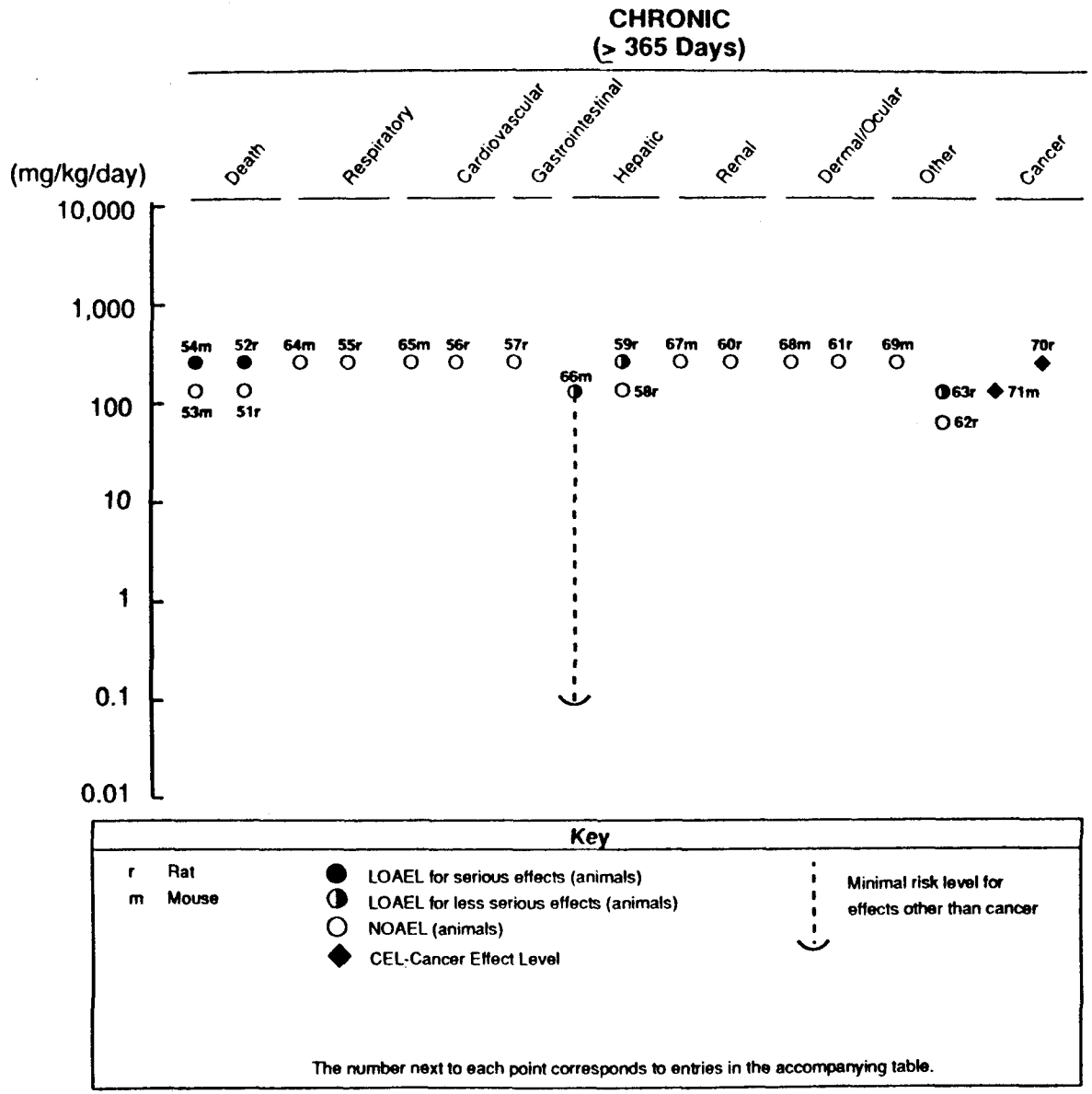


FIGURE 2-2. Levels of Significant Exposure to 1,2 - Dichloropropane - Oral (Continued)

long-term studies of 1,2-dichloropropane administered in food were located; therefore, the dose level of 250 mg/kg/day in mice and rats, which were administered by gavage in corn oil (NTP 1986), were converted to an equivalent concentration of 1900 ppm in food in mice and 5000 ppm in rats, for presentation in Table 1-4.

The highest reliable NOAEL value and all reliable LOAEL values for lethal effects in each species and duration category are reported in Table 2-2 and plotted in Figure 2-2.

2.2.2.2 Systemic Effects

Respiratory Effects. No studies were located regarding respiratory effects in humans following oral exposure to 1,2-dichloropropane.

No histopathologic changes in the lungs were observed in rats treated by gavage in corn oil with up to 1000 mg/kg/day 1,2-dichloropropane for 1, 5, or 10 consecutive days, or with up to 500 mg/kg/day for 13 weeks (5 days/week) (Bruckner et al. 1989). In the gavage studies conducted by NTP (19861, no compound-related histopathological lesions were observed in lungs, bronchi, and trachea of F344/N rats treated with up to 1000 mg/kg/day of 1,2-dichloropropane for 13 weeks, B6C3Fl mice treated with up to 500 mg/kg/day for 13 weeks, or rats and mice treated with up to 250 mg/kg/day for 103 weeks.

The highest reliable NOAEL values for respiratory effects in each species and duration category are reported in Table 2-2 and plotted in Figure 2-2.

Cardiovascular Effects. Death resulting from cardiac failure occurred in two humans 30 and 36 hours after ingestion of single unknown doses of 1,2-dichloropropane (Larcan et al. 1977, Perbellini et al. 1985). A patient in the Perbellini et al. (1985) report showed ecchymoses (a purplish patch caused by extravasation of blood into the skin) on the cheeks, trunk and limbs, and epistaxis (nosebleed) after ingestion of an unknown dose of 1,2-dichloropropane.

Histological examination of the hearts of rats and mice that were treated with doses as high as 250 mg/kg/day (5 days/week) for 103 weeks revealed no compound-related lesions (NTP 1986). The dose of 250 mg/kg/day is reported in Table 2-2 and plotted in Figure 2-2 as a NOAEL for cardiovascular effects in rats and mice as a result of chronic oral exposure.

Gastrointestinal Effects. Chiappino and Secchi (1968) reported a case of acute overexposure by ingestion of 1,2-dichloropropane in which a 59-year-old man experienced an immediate burning sensation in the oropharynx, esophagus, and stomach, followed by vomiting for some time which became biliary vomiting. Nausea, vomiting, and intense anorexia subsided but

persisted over the next 4 days, and the patient ultimately recovered. Perbellini et al. (1985) reported reversible necrotic hemorrhagic lesions in the oral cavity of a man who ingested 1,2-dichloropropane. Thorel et al. (1986) observed reversible erosive esophagitis and esophageal varices in a man who ingested 1,2-dichloropropane in a suicide attempt. The exposures in the above cases were single, but doses were not reported.

Gross pathological lesions were not observed in the gastrointestinal tract of mice or rats that were treated by gavage with 1,2-dichloropropane doses as high as 2000 mg/kg/day for 2 weeks (NTP 1986). The fact that the rats and mice in this study were not examined histologically precludes the use of 2000 mg/kg/day as a NOAEL. Bruckner et al. (1989) observed no histological effects on the stomach in rats treated with 1000 mg/kg/day for 1, 5, or 10 consecutive days.

Rats that were treated with 1,2-dichloropropane doses as high as 1000 mg/kg/day (5 days/week) for 13 weeks and mice similarly treated with up to 500 mg/kg/day did not have histopathological alterations in the gastrointestinal tract (NTP 1986). Similarly, rats treated with up to 500 mg/kg/day for 13 weeks (5 days/week) showed no histopathologic changes in the stomach (Bruckner et al. 1989).

Rats that were treated with 1,2-dichloropropane doses as high as 250 mg/kg/day (5 days/week) for 103 weeks did not have histological alterations in the gastrointestinal tract (NTP 1986). In female mice that were treated by gavage with 1,2-dichloropropane doses of 125 or 250 mg/kg/day (5 days/week) for 103 weeks, increased incidences of acanthosis of the forestomach occurred. In male mice similarly treated, this effect was only observed in the high-dose group. Because it is uncertain whether the acanthosis is compound-related, a LOAEL or NOAEL for gastrointestinal effects as a result of chronic oral exposure to 1,2-dichloropropane cannot be determined for mice.

The highest reliable NOAEL value and all reliable LOAEL values for gastrointestinal effects in each species and duration category *are* reported in Table 2-2 and plotted in Figure 2-2.

Hematological Effects. Anemia, leukopenia and disseminated intravascular coagulation (DIC) occurred in humans after accidental ingestion of 1,2-dichloropropane (Pozzi et al. 1985; Perbellini et al. 1985). One of the patients recovered, one died 7 days after poisoning from septic shock, and one died 30 hours after poisoning from cardiac arrest. These overexposures resulted from a single deliberate ingestion of 1,2-dichloropropane, but doses were not reported.

A dose-related increase in the severity of anemia was found in rats treated with 250 mg/kg/day 1,2-dichloropropane by gavage in corn oil for 1, 5, or 10 consecutive days, and in rats treated with 100 mg/kg/day for 13 weeks (5 days/week) (Bruckner et al. 1989). No anemia was found in rats

treated with 100 mg/kg/day in the acute study. In the intermediate study, anemia was found at the lowest dose level so that a LOAEL of 100 mg/kg/day is defined. No short-term or long-term studies of 1,2-dichloropropane administered in food were located; therefore, the dose level of 250 mg/kg/day in the acute study and of 100 mg/kg/day in the intermediate study were converted to equivalent concentrations of 5000 and 2000 ppm in food, respectively, for presentation in Table l-4. The LOAEL of 100 mg/kg/day for rats in the intermediate study is the lowest effect level (LOAEL or NOAEL) found for any species following intermediate exposure. A LOAEL of 100 mg/kg/day for decreased body weight in rats was also found. Based on the LOAEL of 100 mg/kg/day, an intermediate oral MRL of 0.07 mg/kg/day was calculated as described in the footnote to Table 2-2. This MEL has been converted to an equivalent concentration in food (2.5 ppm) for presentation in Table l-3. The MRL can be compared with existing state and federal criteria levels (see Chapter 7) or to amounts of the chemical encountered in environmental or occupational situations (see Chapter 5).

No compound-related histopathological lesions were observed in the hematopoietic tissues of F344/N rats and B6C3F$_1$ mice treated for 5 days/week with 1,2-dichloropropane at doses of 30-1000 mg/kg/day for 13 weeks or 62-125 mg/kg/day for 103 weeks (NTP 1986). Since clinical hematological tests were not performed, the highest doses in these studies cannot be considered NOAELs for hematological effects.

Musculoskeletal Effects. No studies were located regarding musculoskeletal effects in humans or animals following oral exposure to 1,2-dichloropropane.

Hepatic Effects. Damage to the liver has been reported in people who deliberately drank 1,2-dichloropropane. Liver damage included centrolobular hepatic necrosis (Pozzi et al. 1985), centro- and mediolobular acute hepatic necrosis (Larcan et al. 1977), and acute icteric liver disease in which histological examination and electron microscopy showed diffuse, turbid degeneration in the liver cells, and evident ultrastructural changes in the mitochondria, the endoplasmic reticulum, and the Golgi apparatus (Chiappino and Secchi 1968). Perbellini et al. (1985) reported unspecified liver damage in a man orally overexposed. Thorel et al. (1986) found portal hypertension and histologically, dense, irregular portal fibrosis, which damaged the hepatic parenchyma in a man who ingested 1,2-dichloropropane in a suicide attempt. The aforementioned overexposures resulted from ingestion of a single large dose, but specific amounts were not reported.

In animal studies, the liver has been shown to be affected by acute, intermediate, and chronic oral exposure to 1,2-dichloropropane. Bruckner et al. (1989) reported adverse hepatic effects in rats treated orally for an acute and intermediate period of time. Liver necrosis, characterized by degenerative effects on the centrilobular hepatocytes and mild to moderate hepatitis, was observed in animals treated by gavage with ≥250 mg/kg/day

1,2-dichloropropane in corn oil for 1, 5, or 10 consecutive days. Similar effects (periportal vacuolization and fibroplasia) were found in animals treated with ≥500 mg/kg/day for 13 weeks (5 days/week). No adverse effects, on the rats were found at 100 mg/kg/day in the acute study and at 250 mg/kg/day in the intermediate study. No short-term studies of 1,2-dichloropropane administered in food were located; therefore, the dose level of 250 mg/kg/day in rats, which was administered by gavage in corn oil (Bruckner et al. 1989), was converted to an equivalent concentration of 5000 ppm in food in rats, for presentation in Table l-4. The NTP study (1986) found fatty changes, centrilobular necrosis, and congestion of the liver in rats given 1,2-dichloropropane orally at doses of 1000 mg/kg/day, but not ≤500 mg/kg/day for 13 weeks. Liver lesions were not observed in mice that were similarly treated with doses as high as 500 mg/kg/day (NTP 1986).

The NTP study (1986) found liver necrosis in female rats given 250 mg/kg/day 1,2-dichloropropane by gavage for 103 weeks, but not in females at ≤125 mg/kg/day or in males at any of the doses. The NTP study (1986) found necrosis of the liver in male mice, but not females, that were administered 125 or 250 mg/kg/day 1,2-dichloropropane by gavage for 103 weeks (5 days/week); lower doses were not tested. No long-term studies of 1,2-dichloropropane administered in food were located; therefore, the dose level of 125 mg/kg/day in mice and 250 mg/kg/day in rats, which were administered by gavage in corn oil (NTP 1986), were converted to an equivalent concentration of 960 ppm in food in mice and 5000 ppm in food in rats for presentation in Table l-4. The LOAEL of 125 mg/kg/day for hepatic effects in mice is the lowest LOAEL reported following chronic oral exposure to 1,2-dichloropropane (NTP 1986). A NOAEL of 62 mg/kg/day for effects on body weight in rats is reported (NTP 1986), but factors other than chemical toxicity may affect body weight; therefore, it will not be used as the basis for the MRL. Based on the LOAEL of 125 mg/kg/day, a chronic oral MRL of 0.09 mg/kg/day was calculated as described in the footnote to Table 2-2. The NTP study (1986) denoted that a significant dose-related increase in liver adenomas occurred in male mice treated with 250 mg/kg/day (P=0.017) and in female mice treated with the 125 and 250 mg/kg/day (P=0.102 at both doses) (see Section 2.2.2.8 on carcinogenic effects by oral exposure).

The highest reliable NOAEL value and all reliable LOAEL values for hepatic effects in each species and duration category are reported in Table 2-2 and plotted in Figure 2-2.

Renal Effects. Renal failure was observed in three patients after ingestion of 1,2-dichloropropane (Perbellini et al. 1985, Pozzi et al. 1985, Zedda et al. n.d.). Two of the patients died but renal failure did not appear to be the cause of death; one death was attributed to cardiac arrest and the other to septic shock. Dose information on 1,2-dichloropropane was not provided.

Gross pathologic examinations showed reddened renal medullae in almost all rats that were treated with 2000 mg/kg/day by gavage for 2 weeks, but not at 1000 mg/kg/day or lower doses (NTP 1986). This effect was also observed in mice that were similarly treated at doses of ≥125 mg/kg/day; lower doses were not tested, Histological examinations were not performed. NTP (1986) considered the reddened medullae to be a compound-related, but not an adverse effect. The reddened medullae may have been transient since no effects on the kidney, including the reddened renal medullae, were observed grossly or histologically in mice or rats in the 13-week study or in the 103-week study.

No adverse histopathologic effects on the kidneys were found in rats treated with ≤500 mg/kg/day 1,2-dichloropropane by gavage in corn oil following exposure for 1, 5, or 10 consecutive days or exposure for 13 weeks (5 days/week) (Bruckner et al. 1989). Increased BUN levels, however, were found in animals treated with 1000 mg/kg/day in the acute study.

No treatment-related histopathological kidney lesions were observed in rats or mice treated by gavage with 1,2-dichloropropane doses as high as 1000 mg/kg/day for rats and 500 mg/kg/day for mice in the 13 week study and as high as 250 mg/kg/day for both species in the 103 week study (NTP 1986).

The highest reliable NOAEL value and all reliable LOAEL values for renal effects in each species and duration category are reported in Table 2-2 and plotted in Figure 2-2. Since no histological examination of the kidney was done in the 2 week studies in rats and mice (NTP 1986), it would be inappropriate to consider this study as the basis for a NOAEL.

Dermal/Ocular Effects. No studies were located regarding dermal/ocular effects in humans following oral exposure to 1,2-dichloropropane. .

No treatment-related skin lesions were observed histologically in rats or mice treated with 1,2-dichloropropane by gavage for 13 or 103 weeks (NTP 1986). The highest doses (1000 mg/kg/day for rats, 500 mg/kg/day for mice in the 13-week study; 250 for both species in the 103-week study) are indicated in Table 2-2 and Figure 2-2 as NOAELs for dermal effects as a result of intermediate and chronic oral exposure to 1,2-dichloropropane.

Other Effects. Mean body weight gain was depressed by <10% in male rats treated with ≥500 mg/kg/day, but not ≤250 mg/kg/day, and in female rats treated with ≥1OOO mg/kg/day, but not ≤500 mg/kg/day, for 2 weeks; in male rats treated with ≥500 mg/kg/day, but not ≤250 mg/kg/day, and not in female rats treated with ≥500 mg/kg/day, for 13 weeks; and in male rats treated with ≥125 mg/kg/day, but not 62 mg/kg/day, and in female rats treated with ≤250 mg/kg/day, but not 125 mg/kg/day, for 103 weeks (NTP 1986). Body weight gain was not affected in mice similarly treated (≤2000 mg/kg/day for 2 weeks, ≤500 mg/kg/day for 13 weeks, ≤250 mg/kg/day for 103 weeks) in the NTP (1986) study, A significant dose-related decrease in body weight gain

was observed in rats treated with ≥100 mg/kg/day by gavage in corn oil for 13 weeks (5 days/week) (Bruckner et al. 1989). Since 100 mg/kg/day was the lowest dose tested, no NOAEL for body weight gain was defined. The LOAELs and NOAELs for the three durations are reported in Table 2-2 and plotted in Figure 2-2. No short- or long-term studies of 1,2-dichloropropane administered in food were located; therefore, the dose levels of 250 mg/kg/day (short-term) and 100 mg/kg/day (long-term) in rats, which were administered by gavage in corn oil (Bruckner et al. 1989), were converted to an equivalent concentration of 5000 ppm (short-term) and 2000 ppm (long-term) in food for presentation in Table l-4.

2.2.2.3 Immunological Effects

No studies were located regarding immunological effects in humans following oral exposure to 1,2-dichloropropane.

Histological examination of organs and tissues of the immune system revealed no treatment-related effects in rats or mice treated by gavage with 1,2-dichloropropane on 5 days/week with doses ≥30 mg/kg/day for 13 weeks or ≥62 mg/kg/day for 103 weeks (NTP 1986). Reduced survival of the high-dose females in the 103-week study (see section 2.2.1) may have been due partly to infections of the reproductive system; of the animals that died during the study, 5/11 controls, 9/14 at 125 mg/kg/day, and 14/22 at 250 mg/kg/day had inflammation of the reproductive system. However, it is not known if 1,2-dichloropropane caused an increased susceptibility to infections. No specific immunological tests of rats and mice treated with 1,2-dichloropropane were performed in the NTP (1986) studies. Therefore, LOAELs and NOAELs for immunological effects cannot be determined.

2.2.2.4 Neurological Effects

Symptoms observed in patients lethally exposed to 1,2-dichloropropane include dizziness, headache, disorientation and coma (Larcan et al. 1977; Perbellini et al. 1985; Thorel et al. 1986). The overexposure resulted from a single ingestion, but no doses were determined.

Gorzinski and Johnson (1989) performed a neurotoxicological examination, including a Functional Observational Battery, on rats exposed daily to 1,2-dichloropropane by gavage in corn oil for 2 weeks. After the first dose, clinical signs (blinking, lacrimation, salivation and lethargy) were observed in the treated groups, but by the fifth dose, the treated animals were indistinguishable from the controls. Decreased locomotion in males and a trend towards decreased activity in females were found at ≥300 mg/kg/day. Histological examination of the brain was not done. Bruckner et al. (1989) found a dose-related increase in the severity of CNS depression in rats treated with 100 mg/kg/day 1,2-dichloropropane by gavage in corn oil for 1, 5, or 10 consecutive days. No histopathologic lesions were found in the brain. Therefore, a LOAEL of 100 mg/kg/day from the Bruckner et al. (1989) study and a LOAEL of 300 mg/kg/day from the Gorzinski and Johnson

(1989) study can be defined. No short-term studies -of 1,2-dichloropropane administered in the food were located; therefore, the dose level of 100 mg/kg/day in rats, which was administered by gavage in corn oil (Bruckner, et al. 1989), was converted to an equivalent concentration of 2000 ppm in food for presentation in Table l-4. Bruckner et al. (1989) also observed pronounced CNS depression in rats treated with 500 mg/kg/day by gavage for 13 weeks (5 days/week). The existence of CNS depression at the next lower dose (250 mg/kg/day) was not reported, but 250 mg/kg/day cannot be defined as a NOAEL for neurological effects following intermediate exposure since a LOAEL of 100 mg/kg/day was defined by Bruckner et al. (1989) in the acute study. The LOAEL of 100 mg/kg/day for rats is the lowest adverse effect level for any species following acute oral exposure. Based on this value, an acute oral MRL of 0.1 mg/kg/day was calculated, as described in the footnote in Table 2-2. This MRL has been converted to an equivalent concentration in food (3.6 ppm) for presentation in Table l-3. The MRL can be compared with existing state and federal criteria levels (see Chapter 7) or to amounts of the chemical encountered in environmental or occupational situations (see Chapter 5).

Kirk et al. (1989) performed an observational battery on pregnant female rats that were exposed by gavage to 1,2-dichloropropane during days 6-21 of gestation. The observational battery included observations in pupil size, respiration, movement, skin and hair coat, salivation, lacrimation, and urine and fecal staining. No adverse effects were found in dams exposed to ≤30 mg/kg/day, but at 125 mg/kg/day, decreased movement, muscle tone and extensor thrust reflex, and increased salivation and lacrimation were observed.

NTP (1986) found no treatment-related lesions histologically in the brains of rats and mice treated with doses ≥30 mg/kg/day for 13 weeks or ≥62 mg/kg/day for 103 weeks. Specific tests for neurological effects were not performed, however, precluding the determination of LOAELs and NOAELs from this study.

2.2.2.5 Developmental Effects

No studies were located regarding developmental effects in humans following oral exposure to 1,2-dichloropropane.

An increased incidence of delayed ossification of the bones of the skull was observed in the fetuses of dams treated with 125 mg/kg/day 1,2-dichloropropane by gavage in corn oil during gestation days 6-21 (Kirk et al. 1989). No adverse effects were found in the fetuses of dams treated with ≤30 mg/kg/day. The NOAEL of 30 mg/kg/day and the LOAEL of 125 mg/kg/day are reported on Table 2-2 and plotted on Figure 2-2. No long-term (≥14 days) studies of 1,2-dichloropropane administered in food were located; therefore, the dose level of 125 mg/kg/day in rats, which was administered by gavage in corn oil (Bruckner et al. 1989), was converted to an equivalent concentration of 2500 ppm in food for presentation in Table l-4.

2.2.2.6 Reproductive Effects

No studies were located regarding reproductive effects in humans following oral exposure to 1,2-dichloropropane.

Kirk et al. (1989) administered 1,2-dichloropropane by gavage to pregnant rats during gestation days 6-21. No dose-related effects on the number of pregnancies, the number of implantation sites, the number of resorptions, the gravid uterine weight, or the number of fetuses were found at the highest dose level (125 mg/kg/day).

Testicular degeneration was found in rats treated with 500 mg/kg/day by gavage in corn oil for 1, 5, or 10 consecutive days or for 13 weeks (5 days/week) (Bruckner et al. 1989). The degeneration included reduced sperm production, increased numbers of degenerate sperm and reduced numbers of sperm in the epididymis. These effects were not found at dose levels of ≤250 mg/kg/day. No short-term studies of 1,2-dichloropropane administered in food were located; therefore, the dose level of 500 mg/kg/day in rats, which was administered by gavage in corn oil, was converted to an equivalent concentration of 10,000 ppm in food for presentation in Table l-4.

Increased incidences of suppurative infection of the ovary, uterus, or other organs were found in the female mice treated by gavage with doses of 125 and 250 mg/kg/day for 103 weeks (NTP 1986), but it is not known if these infections were related to 1,2-dichloropropane treatment since controls were also infected. Histological examination of the reproductive organs of the male rats and mice in the 103-week study, and of the higher dosed animals in the 13-week study, revealed no compound-related lesions.

The NOAEL of 125 mg/kg/day (Kirk et al. 1989) for effects on the female reproductive system following intermediate exposure and the NOAEL of 250 mg/kg/day and the LOAEL of 500 mg/kg/day for effects on the male reproductive system following intermediate exposure are reported in Table 2-2 and plotted in Figure 2-2. Since no tests of reproductive function were performed in the NTP (1986) study, it is not appropriate to regard the levels that produced no histopathological lesions as NOAELs.

2.2.2.7 Genotoxic Effects

No studies were located regarding genotoxic effects in humans following oral exposure to 1,2-dichloropropane.

In a dominant-lethal study, male rats were continuously exposed to 1,2-dichloropropane in the drinking water for at least 10 weeks prior to breeding and for 1 week after breeding (Hanley et al. 1989). Two days after exposure was ended, the males were bred with untreated females. No effects on mating performance or fertility in the males, or on the number of

implantations, resorptions, and litter sizes were observed at the highest dose (162 mg/kg/day).

2.2.2.8 Cancer

No studies were located regarding carcinogenic effects in humans following oral exposure to 1,2-dichloropropane.

A marginal but statistically significant increased incidence of adenocarcinomas of the mammary gland was observed in female rats given 250 mg/kg/day 1,2-dichloropropane by gavage for 103 weeks (NTP 1986). NTP (1986) considered this to be equivocal evidence for carcinogenicity. 1,2-Dichloropropane was not found to be carcinogenic in other tissues in the females or in any tissues in similarly treated (62 and 125 mg/kg/day) male rats. The 250 mg/kg/day dose is indicated as a Cancer Effect Level (CEL) in rats in Table 2-2 and is plotted in Figure 2-2.

A dose-related increase in liver adenomas for both male and female mice was observed when treated with 125 or 250 mg/kg/day 1,2-dichloropropane by gavage for 103 weeks (NTP 1986). The incidences were significantly greater than control incidences in high-dose male (34% in treated vs. 14% in control) and in low- and high-dose female groups (10% in both treated groups vs. 2% in control). The incidences of hepatocellular carcinoma were increased in the dosed animals although the increase was not significant. NTP (1986) concluded that there was some evidence for carcinogenicity in male and female mice based on the increased incidences of hepatocellular neoplasms, primarily adenomas. The dose of 125 mg/kg/day is presented as a Cancer Effect Level (CEL) in mice in Table 2-2 and is plotted in Figure 2-2. EPA (1987a) classified 1,2-dichloropropane in Group B2 (i.e., a probable human carcinogen), and derived a q_1^* of 6.8×10^{-2} $(mg/kg/day)^{-1}$ from the data in male mice. This q_1^* corresponds to upper bound individual lifetime cancer risks at 10^{-4} to 10^{-7} risk levels of 1.5×10^{-3} to 1.5×10^{-6} mg/kg/day. The EPA plans to recalculate the q_1^* taking into consideration the life table adjustments; therefore, the cancer risk levels are not plotted in Figure 2-2.

2.2.3 Dermal Exposure

2.2.3.1 Death

No studies were located regarding lethal effects in humans following dermal exposure to 1,2-dichloropropane.

A dermal LD_{50} of 8.75 mL/kg was calculated for rabbits (Smyth et al. 1969). The treatment site was covered with an impervious plastic film for 24 hours following application and the animals were observed for 14 days. The LOAEL of 8.75 mL/kg is reported in Table 2-3.

TABLE 2-3. Levels of Significant Exposure to 1,2-Dichloropropane - Dermal[a]

	Species	Exposure Frequency/ Duration		NOAEL[b]	LOAEL[c] (Effect) Less Serious	LOAEL[c] (Effect) Serious	Reference
ACUTE EXPOSURE							
Death							
	rabbit	24 h				8.75 mL/kg (LD_{50})	Smyth et al. 1969
	rabbit	one dose		3.16 g/kg			Exxon 1982a
Systemic							
	rabbit	one dose	Derm/Oc		3.16 g/kg (erythema)		Exxon 1982a

[a]These levels are not displayed graphically because none of the studies used doses expressed in units of $mg/cm^2/day$.
[b]NOAEL - No Observed Adverse Effect Level
[c]LOAEL - Lowest Observed Adverse Effect Level

2.2.3.2 Systemic Effects

Grzywa and Rudzki (1981) reported 2 cases of dermatitis resulting from dermal exposure to aerosols containing 1,2-dichloropropane [7.4-12.7% 2-dichloropropane, with the remainder consisting of methysilicone oils (3.6-8.5%) and freons 11 and 12 in a 1:l proportion (83.6-84.1%)] in the workplace. In one case, a woman with no family history of allergy was dermally exposed to 1,2-dichloropropane by repeated spraying it during the course of her work. Dermatitis appeared on her right hand after several months of work and recurred several times during 6 years of employment. After stopping work, there was no improvement in her condition; and new areas of dermatitis appeared on her left hand and right foot. Patch tests showed a strongly positive reaction to Siliform AR-1 (an aerosol containing 1,2-dichloropropane) and to 1,2-dichloropropane. Twenty-one other workers who were similarly exposed in her workplace did not develop dermatitis. In the second case, a woman with no family history of allergy was dermally exposed to 1,2-dichloropropane in a similar manner; after 4 years of work, dermatitis appeared on the dorsa of her feet and continued for at least 10 years. The dermatitis was exacerbated in the summer and occasionally appeared on her neck. After 13 years of work, the woman developed hand dermatitis, which receded after she changed her work and was no longer exposed to 1,2-dichloropropane. Patch tests showed a positive response to 1,2-dichloropropane and a negative response to Siliform AR-l. Skin changes were seen in two of 39 other persons exposed in her workplace, but these cases were not documented. No dose information was available for either of the above cases.

No studies were located regarding any other systemic effects in humans following dermal exposure to 1,2-dichloropropane.

No studies were located regarding hepatic, renal, musculoskeletal, or cardiovascular system effects in animals following dermal exposure to 1,2-dichloropropane.

No respiratory, gastrointestinal, or hematological effects were observed upon gross examination of rabbits treated dermally with a single dose of 3.16 g/kg 1,2-dichloropropane (Exxon 1982a). Erythema was observed in rabbits treated in the same experiment. The treatment site was occluded for 24 hours following application, and the animals were examined 14 days following treatment. Since tissues of the respiratory, gastrointestinal and hematological systems were only grossly examined, it would be inappropriate to consider the dose of 3.16 g/kg a reliable NOAEL for these effects. The dose of 3.16 g/kg, however, can be considered a LOAEL for dermal effects in rabbits since erythema was observed upon gross examination (see Table 2-3).

Ocular irritation (redness, iridial irritation, cornea1 ulceration) was seen when an unspecified amount of 1,2-dichloropropane was instilled in the conjunctival sac of rabbits (Exxon 1982b). The 1,2-dichloropropane was

placed in the eye, the upper and lower lids were held together for one second to prevent loss of material, and the animals were observed from 1 hour to 14 days after administration. Since no dose information was available for this study, it would be inappropriate to consider it the basis for a LOAEL.

No studies were located regarding the following effects in humans or animals following dermal exposure to 1,2-dichloropropane:

2.2.3.3 Immunological Effects

2.2.3.4 Neurological Effects

2.2.3.5 Developmental Effects

2.2.3.6 Reproductive Effects

No studies were located regarding reproductive effects in humans following dermal exposure to 1,2-dichloropropane.

No effects on the ovaries were observed upon gross examination of rabbits dermally treated with a single dose of 3.16 g/kg 1,2-dichloropropane (Exxon 1982a). The treatment site was occluded for 24 hours following application and the animals were examined 14 days following treatment. Since the ovaries were only grossly examined, the dose of 3.16 g/kg cannot be considered a NOAEL for reproductive effects.

2.2.3.7 Genotoxic Effects

No studies were located regarding genotoxic effects in humans or animals following dermal exposure to 1,2-dichloropropane.

2.2.3.8 Cancer

No studies were located regarding carcinogenic effects in humans or animals following dermal exposure to 1,2-dichloropropane.

2.3 RELEVANCE TO PUBLIC HEALTH

Death. The few deaths observed in humans as a result of deliberate ingestion of 1,2-dichloropropane were apparently due to toxic effects on the central nervous system, liver, and kidney (Pozzi et al. 1985; Larcan et al. 1977; Zedda et al. (n.d.); Perbellini et al. 1985). The ultimate cause of death has been reported to be cardiac arrest and septic shock. No deaths have been reported resulting from inhalation or dermal exposure to 1,2-dichloropropane. All of the documented human overexposures resulted from ingestion or inhalation of 1,2-dichloropropane in the form of a cleaning solvent. Since the use of 1,2-dichloropropane as a consumer cleaning solvent has been curtailed, documented overexposures may be rare in the

future. Information on human lethality resulting from repeated exposures to 1,2-dichloropropane has not been reported.

Doses causing death in animals have been reported for acute and intermediate inhalation exposures, for acute, intermediate, and chronic oral exposure, and for acute dermal exposure. In general, mice were more sensitive to the lethal effects of acute oral exposure to 1,2-dichloropropane than are other laboratory animals. This difference in sensitivity was not found following acute inhalation exposure. During intermediate or chronic oral or inhalation exposure, mice and rats were equally sensitive (NTP 1986; Nitschke et al. 1988). The reason for this difference in sensitivity is not known; and it is not clear if humans are more or less sensitive to 1,2-dichloropropane in relation to other animals, since dose information is not available for the cases of human overexposure. Conventionally, it is assumed that humans are as sensitive as the most sensitive species tested when assessing the risk of 1,2-dichloropropane lethally to humans. The concentrations associated with death in animals are much higher than would be found in the environment, in occupational settings, or in water or soil surrounding waste sites; therefore, it is unlikely that humans would die from noncancer effects after brief or prolonged exposure to 1,2-dichloropropane in air, food, water, or soil. 1,2-Dichloropropane has been rated a B2 carcinogen, however, so prolonged exposure could result in death from cancer.

Systemic Effects. Systemic effects of 1,2-dichloropropane include respiratory effects due to irritation of the respiratory tract, hematological effects, and hepatic and renal alterations manifested primarily as fatty degeneration.

Respiratory effects, including chest discomfort, dyspnea and cough, were reported in humans as a consequence of inhalation exposure to 1,2-dichloropropane (Rubin 1988); respiratory effects have not been observed in humans following oral or dermal exposure. Similarly, respiratory effects in animals were seen only as a result of inhalation exposure. Following inhalation exposure, rats appeared to be more sensitive to the effects of 1,2-dichloropropane on the nasal tissues than mice (Nitschke et al. 1988). This sensitivity was observed following both acute and intermediate exposure (Nitschke and Johnson 1983; Nitschke et al. 1988).

Cardiac failure was the cause of death for 2 patients who ingested a single dose of 1,2-dichloropropane (Larcan et al. 1977; Perbellini et al. 1985). It is likely, however, that the cardiac failure in humans is a result of toxicity to the CNS. Oral studies in animals did not show cardiovascular effects resulting from 1,2-dichloropropane, but this may be a consequence of the limited scope of pathological examination in the high dose acute studies. Human inhalation studies did not report adverse effects on the cardiovascular system. Animal inhalation studies by Heppel et al. (1946), however, reported some fatty degeneration of the heart, but this effect was only seen in the animals that died. Similar effects,

however, were not observed in more recent studies by Nitschke and coworkers (Nitschke and Johnson 1983; Nitschke et al. 1988).

Adverse gastrointestinal effects were seen in humans after deliberate inhalation and ingestion of 1,2-dichloropropane (Pozzi et al. 1985; Chiappino and Secchi 1968; Perbellini et al. 1985). These effects included nausea, vomiting and gastrointestinal tract lesions. Nausea and vomiting are general effects that could very well be due to CNS toxicity.; therefore, it is difficult to determine if these effects are secondary to the gastrointestinal irritation/corrosion or CNS toxicity. Acanthosis of the forestomach was seen in mice in a chronic oral study done by NTP (1986), but no effects on the gastrointestinal system were seen in any inhalation studies. The acanthosis may be a consequence of repeated ingestion of an irritant which is consistent with the gastrointestinal effects of 1,2-dichloropropane on humans. It was not clear that the acanthosis was specifically due to 1,2-dichloropropane.

Disseminated intravascular coagulation (DIC) and hemolytic anemia were found in humans as a result of overexposure to 1,2-dichloropropane (Perbellini et al. 1985; Pozzi et al. 1985). This finding, somewhat unusual in cases of solvent exposure, was reported in a total of five patients between the two studies regardless of route of exposure (inhalation or ingestion). Perbellini et al. (1985) suggested that hemolysis resulting from 1,2-dichloropropane may trigger DIC, but the mechanism has yet to be proven. In animal studies, a dose-related increase in the severity of anemia was found in rabbits exposed to 1,2-dichloropropane by inhalation (≥150 ppm, 6 hours/day, 5 days/week, 13 weeks) (Nitschke et al. 1988) and in rats treated orally with 1,2-dichloropropane (≥250 mg/kg/day for up to 10 consecutive days and at ≥100 mg/kg/day, 5 days/week for 13 weeks) (Bruckner et al. 1989). These results are consistent with the anemia observed in humans as a result of both inhalation and ingestion of 1,2-dichloropropane.

One of the principal target organs, in both animals and humans, for the toxicity of 1,2-dichloropropane is the liver. The major effects in both animals and humans resulting from both inhalation and oral exposure are fatty degeneration and necrosis. The hepatic effects of 1,2-dichloropropane on humans result from unknown, but apparently high, doses either ingested in a single bolus dose or inhaled over a short period of time.

Secchi and Alessio (1968, 1971) reported increases in hepatic enzymes found in human serum as an indicator of hepatic damage resulting from ingestion of 1,2-dichloropropane (mixture of 70% 1,2-dichloropropane and 30% trichloroethylene). Cytoplasmic liver enzymes found in the serum indicated less severe damage to hepatocytes, while mitochondrial and lysosomal liver enzymes found in the serum indicated severe hepatic damage, usually associated with death (3/6 subjects died). Compound-related damage to mitochondrial structures results in the depression of metabolic processes related to the production of energy, and damage to the lysosomes results in the release of hydrolytic enzymes into the cell which is responsible for

fatal cellular necrosis. In this study, histological examination of the liver of the patients positively correlated with the serum-enzymological findings.

Bonashevskaya et al. (1976) discussed a proposed mechanism of action of 1,2-dichloropropane on the rat liver based on work done on chlorinated aromatic compounds. The centrolobular region of the liver was reported as the focus for detoxification of lipophilic substances, while the peripheral region of the liver manages the elimination of toxins with the bile. The toxic effects of 1,2-dichloropropane are generally localized in the centrolobular region of the liver. The 1,2-dichloropropane penetrates the plasma membranes in the centrolobular region and is metabolically transformed because of the activity of microsomal enzymes. This system of microsomal enzymes is also described by Van Dyke and Wineman (1971) (see section 2.3.1.3 on Metabolism). The activation of the enzyme system results in hyperplasia of the endoplasmic reticulum, resulting in the loss of ribosomes. The loss of the ribosomes results in a decrease in protein synthesis and, therefore, an inhibition of lipoprotein formation. Consequently, lipid inclusions appear in the cytoplasm of the cells, resulting in fatty degeneration of the liver. This mechanism has been proposed in the literature but has yet to be completely proven, and the relevance of the mechanism to humans remains unknown.

Renal failure has occurred in people exposed to 1,2-dichloropropane orally and by inhalation (Pozzi et al, 1985; Zedda et al. (n.d.); Perbellini et al. 1985). Fatty degeneration of the kidney was seen in animals exposed by inhalation to 1,2-dichloropropane (Highman and Heppel 1948). Reddened renal medullae were found in animals treated by gavage for 2 weeks, but was not found in animals treated for longer time periods (NTP 1986). The reddened medullae may be transient lesions that disappear after initial exposure to 1,2-dichloropropane. The animal inhalation and oral studies suggest that kidney toxicity may be a consequence of single and repeated exposure to 1,2-dichloropropane.

Dermal/ocular effects of 1,2-dichloropropane have occurred in humans; these include periorbital and conjunctival hemorrhages following vapor exposure (Pozzi et al. 1985) and dermatitis after dermal exposure (Grzywa and Rudzki 1981). Conjunctivitis was seen in guinea pigs exposed to 1,2-dichloropropane vapor (Heppel et al. 1946), but no dermal/ocular effects were seen as a result of oral exposure. These local irritative effects of 1,2-dichloropropane are consistent with the gastrointestinal tract data; the chemical appears to be a local irritant by all routes, as might be expected.

The reported systemic effects of 1,2-dichloropropane in humans have resulted from inhalation or ingestion of 1,2-dichloropropane in the form of a cleaning solvent, or from dermal contact with aerosols in the workplace. Since 1,2-dichloropropane is no longer available as a consumer solvent, and its use as an industrial solvent involves closed systems, the potential for human exposure is minimal. The concentrations associated with systemic

effects in animals are much higher than those found in the environment, in occupational settings, or in water or soil surrounding waste sites, so it is not likely that harmful, noncancer effects would result from brief or prolonged human exposure to 1,2-dichloropropane in air, food, water, or soil. 1,2-Dichloropropane has been rated a B2 carcinogen, however, so prolonged exposure may result in cancer.

Immunological Effects. Sensitization has occurred in humans dermally exposed to 1,2-dichloropropane in the workplace (Grzywa and Rudzki 1981) (see Section 2.2.3.2). Immunological effects in humans have not been observed as a result of oral or inhalation exposure. An in vitro study on the toxicity of 1,2-dichloropropane on human lymphocytes was conducted by Perocco et al. (1983). The cellular parameters studied included tritiated thymidine uptake and viability in cells grown with or without the S-9 rat liver metabolizing system. The S-9 liver system is included to provide mammalian liver enzymes that may be necessary to metabolize the compound being tested into a more or less toxic chemical, simulating events in vivo. No cytotoxic action against human lymphocytes was seen as a result of exposure to 1,2-dichloropropane. Dermal exposure in humans may result in immunological effects, but it is inappropriate to draw any conclusions regarding other routes of exposure due to the limited data. In mice, a decrease in the absolute and relative thymus weight and a decrease in cortical lymphoid cells were found in animals exposed by inhalation to 300 ppm 1,2-dichloropropane (6 hours/day, 5 days/week, 2 weeks) (Nitschke and Johnson 1983). Except for the acutely exposed mice described above (Nitschke and Johnson 1983), no changes in the immunological organs or tissues were observed in animals exposed by inhalation (acute or intermediate exposure periods) or treated orally (intermediate and chronic exposure periods). Tests of immunological function were not performed following any route of exposure in animals.

Neurological Effects. The CNS is a principal target for 1,2-dichloropropane toxicity. Dizziness, disorientation, and coma are some of the effects on the central nervous system which have occurred in humans after overexposure by ingestion (Larcan et al. 1977; Perbellini et al. 1985; Thorel et al. 1986). The dose-response relationship for this effect cannot be characterized due to lack of quantitative dose information. Reported neurological effects resulting from inhalation exposure were less pronounced than the effects resulting from oral exposure, probably due to different exposure levels. Since only two case studies of inhalation overexposure are available (Pozzi et al. 1985; Rubin 1988) and since CNS effects as a result of oral overexposure to high levels are severe, it is reasonable to assume that inhalation exposures (at concentrations that would result in the same internal dose as in the oral studies), may produce CNS effects of similar severity to those found in the oral studies. The mechanism of action on the CNS has not been determined, but Perbellini et al. (1985) found a high concentration of 1,2-dichloropropane in the brain of a woman who died following ingestion of 1,2-dichloropropane. In animal studies, neurological effects (lethargy, CNS depression, decreased activity) were found following

acute inhalation exposure (Nitschke and Johnson 1983) and following acute and intermediate oral exposure (Gorzinski and Johnson 1989; Bruckner et al. 1989). These observations are consistent with the effects found in humans following both inhalation and ingestion of 1,2-dichloropropane.

Since 1,2-dichloropropane is no longer available as a consumer solvent, it is unlikely that other modes of human exposure (air, food, or water) would result in harmful central nervous system effects.

Genotoxic Effects. No studies were located regarding genotoxic effects in humans or animals following inhalation or dermal exposure to 1,2-dichloropropane. In an oral dominant-lethal study in mice, no effects were found on mating performance or fertility in the males, or on the number of implantations, resorptions, and litter sizes (Hanley et al. 1989). Results of in vitro genetic testing of 1,2-dichloropropane are presented in Table 2-4. A number of investigators found that 1,2-dichloropropane is mutagenic for various strains of Salmonella, when tested with or without S-9 exogenous metabolic activation preparation. Carere and Morpurgo (1981) and Principe et al. (1981) found that 1,2-dichloropropane was mutagenic for Aspergillus but not Streptomyces when tested without an exogenous metabolic activation system. 1,2-Dichloropropane was mutagenic in mouse lymphoma cells when tested with exogenous activation (Tennant et al. 1987) and in Drosophila (exposed by inhalation and ingestion) (Woodruff et al. 1985). Chromosomal aberrations were induced in Chinese hamster ovary cells under both activated and non-activated conditions, but not in Aspergillus (Crebelli et al. 1984). Since 1,2-dichloropropane is mutagenic in bacteria, mouse lymphoma cells and Drosophila, and clastogenic in Chinese hamster cells, it is appropriate to predict that 1,2-dichloropropane poses a genotoxic threat to humans.

Cancer. Chronic oral exposure to 1,2-dichloropropane produced significantly increased incidences of hepatocellular neoplasms in male and female mice and mammary gland adenocarcinomas in female rats (NTP 1986). Male mice of the strain used (B6C3Fl) in the NTP (1986) study are known to have a high incidence of benign liver tumors. The normally high rate of these tumors can be enhanced by various stimuli including stress, irritants, carcinogenic chemicals and promoters. As discussed by NTP (1986), promoters seem to enhance the incidence of liver tumors only in animals that have a high spontaneous rate. Carcinogenic chemicals, however, have increased the incidence of both benign and malignant liver tumors in mice, regardless of whether a certain strain has a high incidence of spontaneous tumors. NTP (1986) discussed the possibility that 1,2-dichloropropane was a tumor promotor but could not come to a conclusion.

NTP (1986) regarded the increased incidences of mammary gland adenocarcinoma in female rats as equivocal evidence of carcinogenicity. That the increase was associated with 1,2-dichloropropane exposure is strengthened by the following facts: these are relatively rare tumors in the strain of rat used; the incidence was 25% in the high-dose females that

TABLE 2-4. Genotoxicity of 1,2-Dichloropropane

Endpoint	Species	Activation	Result	Reference
Gene mutation	Salmonella	+	+	Haworth et al. 1983
		-	+	Principe et al. 1981 Zeiger 1987 Carere et al. 1981 Tennant et al. 1987 Stolzenberg et al. 1980; NTP 1986
	Streptomyces	NT	-	Carere et al. 1981; Principe et al. 1981
	Aspergillus	NT	+	Carere et al. 1981; Principe et al. 1981
	Drosophila	NA	+	Woodruff et al. 1985
	Mouse lymphoma cells	+	+	Tennant et al. 1987
		-	-	
Chromosomal aberrations	Aspergillus	NT	-	Crebelli et al. 1984
	Chinese hamster ovary cells	+	+	von der Hude et al. 1987; Galloway et al. 1987; Tennant et al. 1987; NTP 1986
		-	+	
Dominant lethal	Rat	NA	-	Hanley et al. 1989

NT = Not tested
NA = Not applicable

survived until the end of the study; and the lower body weight of the high-dose females would be expected to decrease the spontaneous rate, rather than enhance it. However, the toxicity of the high dose may have affected the homeostasis of the female rats; the incidence of mammary fibroadenomas was decreased in the high-dose females relative to controls, and the adenocarcinomas were morphologically similar to tumors classified by some pathologists as highly cellular fibroadenomas.

The EPA (1987b) has classified 1,2-dichloropropane as a B2 carcinogen (probable human carginogen) based on the NTP (1986) study, which concluded that 1,2-dichloropropane is reasonably anticipated to be a human carcinogen.

2.4 LEVELS IN HUMAN TISSUES AND FLUIDS ASSOCIATED WITH HEALTH EFFECTS

No studies were located that associated human tissue levels with human health effects or with environmental levels of 1,2-dichloropropane.

Perbellini et al. (1985) described a case of oral overexposure to 1,2-dichloropropane where the subject died from cardiac arrest 30 hours after ingestion. Symptoms of the overexposure included; initial agitation, bradycardia, hypertension and anuria, followed by hypoxemia, shock, DIC and cardiac arrest. Approximately 28 hours after ingestion, 7614 µg/L of 1,2-dichloropropane was found in the subject's blood and, after 29 hours, the concentration found was 6900 µg/L. At autopsy, the concentration of 1,2-dichloropropane was determined in several tissues; brain tissue contained 18,005 µg/L, cerebellar tissue contained 39,890 µg/L and adipose tissue contained 531,840 µg/L.

2.5 LEVELS IN THE ENVIRONMENT ASSOCIATED WITH LEVELS IN HUMAN TISSUES AND/OR HEATH EFFECTS

Rubin (1988) described health effects as a result of an accidental spill of 2000 gallons of 1,2-dichloropropane in 1981. The complaints from those exposed included chest discomfort, dyspnea, and a cough, suggesting that 1,2-dichloropropane is a respiratory tract irritant. The concentration of 1,2-dichloropropane in the air was not determined, so the health effects cannot be correlated level.

Amoore and Hautala (1983) odor thresholds of 214 industrial chemicals, including 1,2-dichloropropane, and compared these values with the Threshold Limit Values (TLV) recommended by the ACGIH. The air odor threshold of 1,2-dichloropropane is 0.25 ppm. The study reported that 50-90% of distracted persons would perceive the odor of 1,2-dichloropropane at the TLV of 75 ppm. The experiment was done with distracted persons, and not persons focused on detecting an odor, in order to better simulate the work environment. It is likely that unacclimated people would smell 1,2-dichloropropane before experiencing significant exposure.

Ghittori et al. (1987) evaluated the Biological Equivalent Exposure Limit (BEEL) for nine solvents, including 1,2-dichloropropane. BEEL refers to the concentration of a substance in a biological compartment when the environmental exposure level through the lungs equals the Threshold Limit Value (TLV). Ghittori et al. (1987) used urinary concentration of 1,2-dichloropropane as a biological indicator and correlated it with the TLV. A linear relationship between breathing zone concentration and urinary concentration was obtained. This relationship is displayed graphically in Figure 2-3.

Cramer et al. (1988) introduced a method for the detection of volatile compounds, including 1,2-dichloropropane, at parts per trillion (ppt) levels in whole blood (see Table 6-l). This method was validated using blood samples from a small population. Based on the method validation data, this method appears reliable and, in the future, may be routinely used to detect organic chemicals in human whole blood.

Wallace et al. (1982) monitored 1,2-dichloropropane and other volatile organic compounds in the breathing-air zone, in drinking water and in exhaled breath at a petrochemical area in Texas and in a non-industrial area in North Carolina. In this study, it was determined that inhalation was the main route of exposure to volatile organic compounds. No 1,2-dichloropropane, however, was found in the ambient air or in expired breath at either test site.

2.6 TOXICOKINETICS

2.6.1 Absorption

2.6.1.1 Inhalation Exposure

No studies were located regarding the rate and extent of absorption of 1,2-dichloropropane following inhalation exposure of humans. During the first 24 hours after a 6-hour exposure of rats to ^{14}C-1,2-dichloropropane (5, 50, or 100 ppm), 71-88% of the recovered dose was found in the excreta, with 55-65% of the recovered dose found in the urine and 16-23% of the recovered dose found in expired air as $^{14}CO_2$ (Timchalk et al. 1989). These data suggested that 1,2-dichloropropane was absorbed through the lungs. The data indicated that 1,2-dichloropropane was rapidly absorbed according to a zero-order input, but that absorption was not linear with respect to the concentration of 1,2-dichloropropane. The authors assumed that 60% of the inspired concentration of ^{14}C-1,2-dichloropropane was absorbed, but the basis for this assumption was not reported (Timchalk et al. 1989). Sato and Nakajima (1979) measured the blood/air partition coefficient of 10.7 for 1,2-dichloropropane indicating that 1,2-dichloropropane is readily absorbed from the lungs.

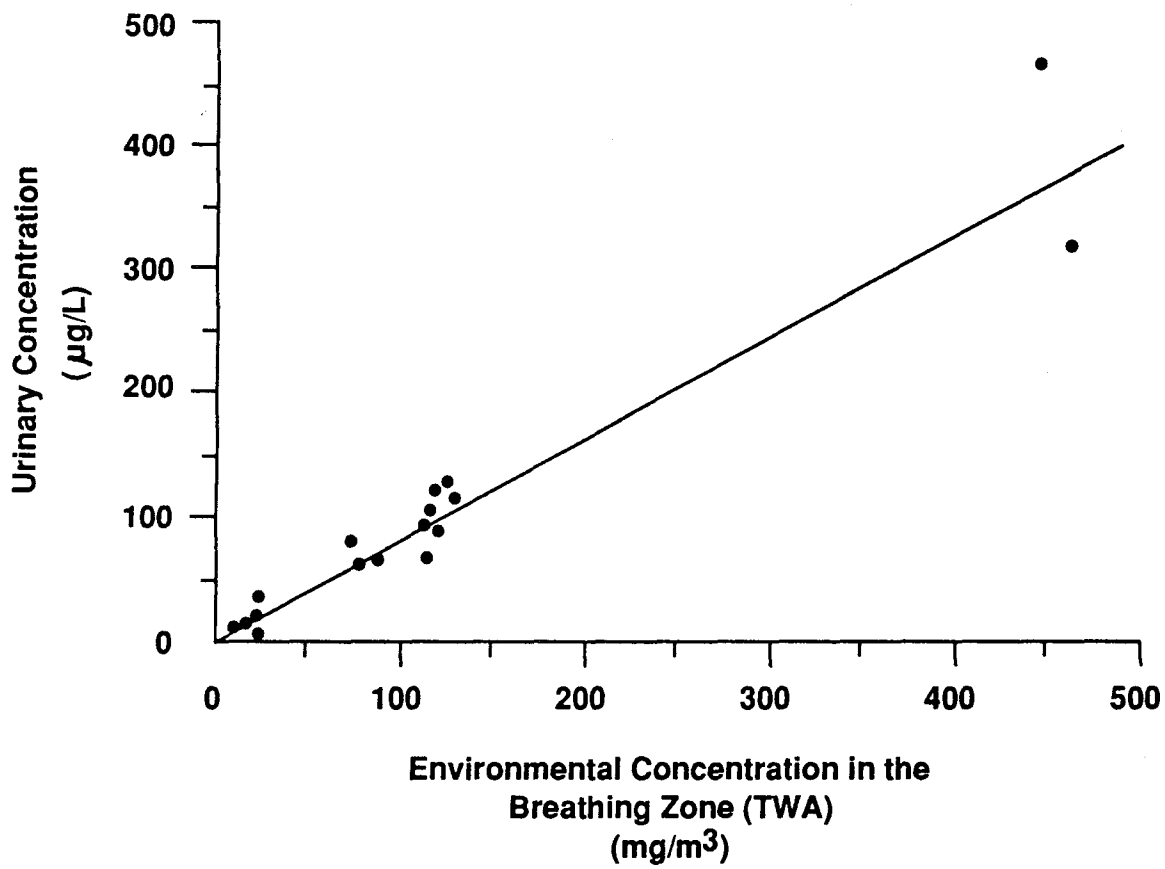


FIGURE 2-3. Relationship Between Breathing Zone Concentration of 1,2-Dichloropropane and Urinary Concentration

Source: Ghittori et al. 1987

2.6.1.2 Oral Exposure

No studies were located regarding the rate and extent of absorption of 1,2-dichloropropane following oral exposure of humans. Studies in rats by Hutson et al. (1971) and Timchalk et al. (1989), which found that an average of 74-95% of the ^{14}C-labeled 1,2-dichloropropane dose was excreted in the urine or in expired air within 24 hours of dosing, suggest that 1,2-dichloropropane is readily and extensively absorbed from the gastrointestinal tract. This is supported by the fact that only 0.5% of the administered dose remained in the gut 4 days after administration (Hutson et al. 1971).

2.6.1.3 Dermal Exposure

No studies were located regarding the rate and extent of absorption of 1,2-dichloropropane following dermal exposure of humans or animals. That 1,2-dichloropropane is absorbed by the skin can be inferred from the lethality observed in rabbits following dermal exposure (see section 2.2.3.1 on Death following dermal exposure).

2.6.2 Distribution

2.6.2.1 Inhalation Exposure

After rats were exposed for 6 hours to 5, 50, or 100 ppm ^{14}C-labeled 1,2-dichloropropane, the radioactivity was well distributed among the major tissues, with the highest concentration in the liver, kidney, lung, and blood (Timchalk et al. 1989).

2.6.2.2 Oral Exposure

Perbellini et al. (1985) described a case of a lethal overdose from a single ingestion of 1,2-dichloropropane. Death occurred 30 hours after ingestion. At autopsy, 18,005 µg/L 1,2-dichloropropane was found in the brain tissue, 39,890 µg/L was found in the cerebellar tissue, and 531,840 µg/L was found in adipose tissue.

Timchalk et al. (1989) observed that 48 hours after administration of ^{14}C-labeled 1,2-dichloropropane, the radioactivity was well distributed among the major tissues, with liver having the highest concentration. The distribution of radioactivity in the tissues of rats was similar following inhalation and oral exposure to 1,2-dichloropropane in the Timchalk et al. (1989) study, with the exception of high levels of radioactivity found in the lungs only after inhalation exposure. In a study by Hutson et al 1971), rats were administered one dose of 4.0 mg kg 1,2-dichloro(l-^{14}C)propane. Approximately 1.5% and 3.5% of the ^{14}C dose were found in the skin and carcass, respectively, after 96 hours.

2.6.2.3 Dermal Exposure

No studies were located regarding the distribution of 1,2-dichloropropane following dermal exposure.

2.6.3 Metabolism

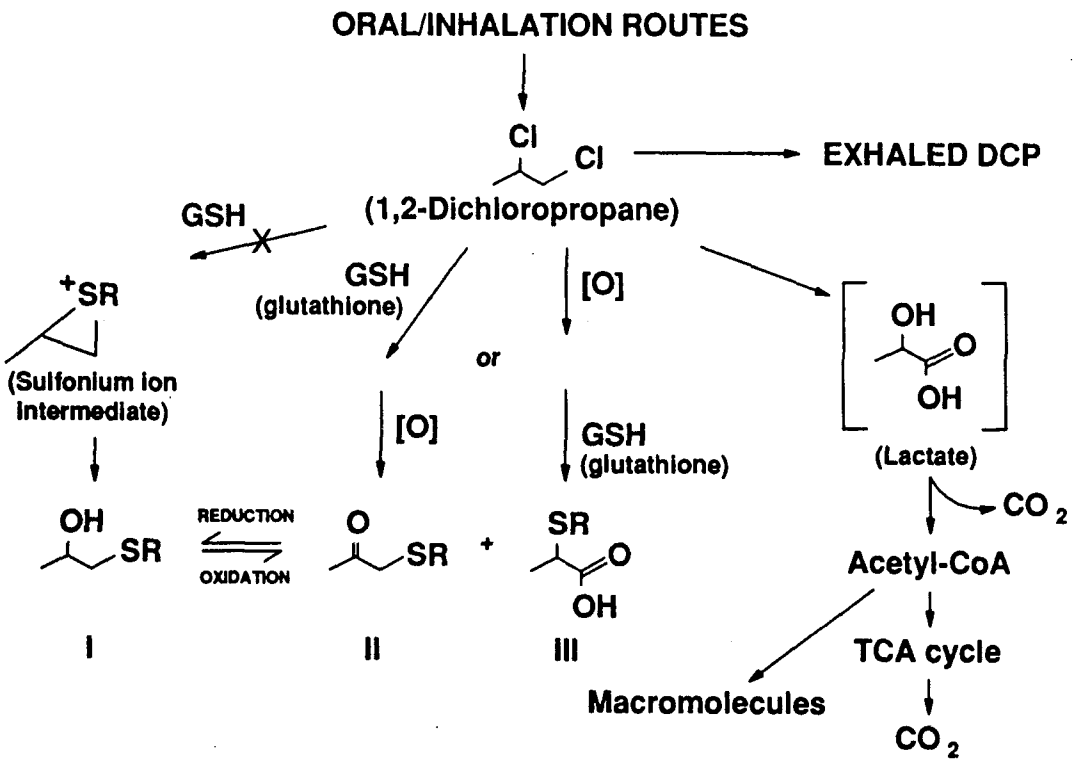
No studies were located regarding the metabolism of 1,2-dichloropropane following dermal exposure in humans or in animals.

Hutson et al. (1971) administered 4.8 mg/kg 1,2-dichloro(l-^{14}C)propane orally to rats and 42.4% of the given dose was measured in the expired air after 96 hours. Of the 42.4%, 19.3% was expired as (^{14}C)C0$_2$, indicating that extensive metabolism of 1,2-dichloropropane had occurred.

Jones and Gibson (1980) administered one dose of 100 mg/kg/day intraperitoneally to rats and measured the amount of 1,2-dichloropropane in the expired air, They found 5% of the administered dose after 0-3 hours, and 5% of the dose after 9-18 hours, indicating that the 1,2-dichloropropane is transported in the blood and expired by the lungs.

Timchalk et al. (1989) described the time course of 1,2-dichloropropane in the blood as a one-compartment open pharmacokinetic model, with zero-order input and first-order elimination. In rats exposed to 50 or 100 ppm 1,2-dichloropropane vapors for 6 hours, the peak blood concentrations were 17- to 19- and 68- to 84-fold higher, respectively, than the peak blood concentration of the 5 ppm group. This dose-dependent non-linearity of blood clearance suggests that metabolism and/or elimination of 1,2-dichloropropane becomes saturated with increasing concentrations (Timchalk et al. 1989).

The major urinary metabolites in rats treated by gavage or exposed to 1,2-dichloropropane vapors are N-acetyl-S-(2-hydroxypropyl)-L-cysteine, N-acetyl-S-(2-oxopropyl)-L-cysteine, and N-acetyl-S-(l-carboxyethyl)-Lcysteine. These metabolites accounted for approximately 84% of the urinary metabolites excreted (Timchalk et al. 1989) (see Figure 2-4). Data indicate that the three N-acetyl cystein conjugates result from 1,2-dichloropropane undergoing oxidation, either before or after conjugation with gluathione. The data also indicate that 1,2-dichloropropane may conjugate with lactate, forming CO_2 and Acetyl Co-A. Acetyl Co-A may then enter the TCA cycle and generate more CO_2 or may be utilized in various biosynthetic pathways. In another study, 25-35% of an oral dose of 20 mg/kg/day 1,2-dichloropropane administered for 4 days was excreted as N-acetyl-S-(2-hydroxypropyl)-cysteine. β-Chloroactate and N-acetyl-S-(2,3-dihydroxypropyl)-cysteine were also detected in the urine (Jones and Gibson 1980). Similar urinary metabolites (mercapturic acids) were detected following intraperitoneal administration of 1,2-dichloropropane (Trevisan et al. 1988).



I = N-acetyl-S-(2-hydroxypropyl)-L-Cysteine
II = N-acetyl-S-(2-oxopropyl)-L-Cysteine
III = N-acetyl-S-(1-carboxyethyl)-L-Cysteine

Figure 2-4. Proposed Metabolic Scheme for 1,2-Dichloropropane in the Rat (R = N-acetylcysteine).

Repeated exposure of rats to 1 mg kg/day 1,2-dichloropropane via gavage for 7 days following a single dose of ^{14}C-labeled compound resulted in enhanced oxidative metabolism (increased CO_2 formation) and reduced radioactivity excreted in the urine compared to rats receiving only the single-labeled dose (Timchalk et al. 1989).

Van Dyke and Wineman (1971) determined that 5.8% of (^{36}Cl)1,2-dichloropropane was enzymatically dechlorinated in vitro by an enzyme system found in hepatic microsomes. This system required NADPH and oxygen and was inducible by phenobarbital and benzpyrene, but not by methylcholanthrene. The optimum pH of the system was 8.2.

2.6.4 Excretion

2.6.4.1 Inhalation Exposure

In rats exposed to 5, 50, or 100 ppm of ^{14}C-labeled 1,2-dichloropropane vapors for 6 hours, the principal routes of elimination were the urine and expired air; 55-65% of the recovered does was excreted in the urine, expired CO_2 accounted for 16-23% of the recovered dose, and 1.7, 2.1-3.4, and 6.3-6.7% of the recovered dose was expired as organic volatiles in the 5, 50, and 100 ppm groups, respectively. The majority of the administered dose was excreted within the first 24 hours after exposure (Timchalk et al. 1989).

2.6.4.2 Oral Exposure

In a study by Hutson et al. (1971), rats were administered one dose of 4.0 mg/kg 1,2-dichloro(1 -^{14}C)propane by gavage. In the first 24 hours, 80-90% of the ^{14}C dose was excreted in the urine, feces, and expired air. After 24 hours, males had excreted 48.5% of the dose in the urine and 5.0% of the dose in the feces. Females had excreted 51.9% of the dose in the urine and 3.8% of the dose in the feces in the same time period. Therefore, the percentage of radioactivity in expired air after 24 hours ranged from 24.3-36.5% of the dose in both sexes. Similar results were observed in rats administered 1 or 100 mg/kg of ^{14}C-labeled 1,2-dichloropropane (Timchalk et al. 1989). In a separate experiment, 42.4% of the administered ^{14}C dose of 4.8 mg/kg 1,2-dichloro(l-^{14}C)propane was detected in the expired air after 96 hours (Hutson et al. 1971).

In rats exposed to 1 mg/kg of ^{14}C-labeled 1,2-dichloropropane, 31-36% of the dose was expired as CO_2 and 0.14-1.13% as volatile organics. In animals treated with 100 mg/kg, 23-27% of the label was expired as CO_2 and 10-16% as volatile organics. The differences between the two groups were statistically significant. In the 100 mg/kg groups, 82% of the exhaled volatile organics were identified as 1,2-dichloropropane (Timchalk et al. 1989).

Trevisan et al. (1988) administered 1,2-dichloropropane intraperitoneally to rats and determined that it is excreted in the urine in

the form of mercapturic acids, N-acetyl-S-(2-hydroxypropyl)cysteine and N-acetyl-S-(2,3-dihydroxypropyl)cysteine. A non-linear, dose-dependent excretion was observed with the maximum excretion seen 9 hours after injection.

2.6.4.3 Dermal Exposure

No studies were located regarding the excretion of 1,2-dichloropropane following dermal exposure.

2.7 INTERACTIONS WITH OTHER CHEMICALS

A common soil fumigant known as D-D consists of 1,2-dichloropropane (27.1%), 1,3-dichloropropene (53%), related compounds and 1% epichlorohydrin. Nater and Gooskens (1976) reported three incidences of exposure to D-D which resulted in dermatosis. Patch testing suggested the existence of a contact allergic sensitivity to D-D in one of the patients. Patch tests with components of D-D suggest that the cause of the contact allergy is with the dichloropropene component.

Shell Oil Co. (1982) studied the toxic effects of 1,2-dichloropropane (light ends) which is a mixture of 65% 1,2-dichloropropane and various other dichloropropane/dichloropropenes. The oral LD_{50} in rats was 487 mg/kg (95% confidence limits, 387-613 mg/kg), which was found in fairly good agreement with the LD_{50} value of 604 mg/kg, calculated on the basis of the additive effects of the major components of the mixture, indicating that potentiation of toxicity was not occurring. The 24-hour percutaneous LD_{50} in rats was greater than 2340 mg/kg (the maximum dose volume that could be applied). The Draize skin irritancy test showed necrosis of female rabbit skin with a less severe effect seen in males. In both sexes, skin reactions persisted at 21 days after dosing. The mixture was mildly irritating to rabbit eyes with a severe initial pain reaction. The mixture was a strong sensitizer in guinea pigs (19/20 positive after 24 hours, 16/20 after 48 hours).

Shell Oil Co. (1983) studied the genotoxic effects of a mixture of dichloropropanes and dichloropropenes in which 1,2-dichloropropane was the major component (65%). Compound-related effects were observed with several strains of Salmonella that contained base substitution mutations, and with Saccharomyces. Similar effects were found with 1,3-dichloropropene (25% of mixture), indicating that the mutagenic response may have been due to 1,3-dichloropropene. The mixture did not mutate rat liver cells (RL4) in vitro.

Parker et al. (1982) exposed CD-1 mice and F344 rats to mixtures of D-D [1,3-dichloropropene (52%)/1.2-dichloropropane (29%)] at concentrations of 0, 5, 15 or 50 ppm, 6 hours/day, 5 days/week for 6 or 12 weeks. Exposure-related effects in the animals exposed to 50 ppm D-D included increased mean liver/body weight ratios in male rats, increased mean kidney/body weight ratios in female rats and slight to moderate diffuse hepatic enlargement in

male mice after 12 weeks of exposure. No exposure-related effects were found at the lower exposure levels.

Linnett et al. (1988) studied the effects of subchronic inhalation of D-D (1,3-dichloropropene (53.7%)/1,2-dichloropropane(25.6%)) on reproduction in male and female rats. Exposures up to 90 ppm for 10 weeks had no effects on the libido, fertility, or morphology of the reproductive tracts of male or female rats.

In animals, the joint toxicity of 1,2-dichloropropane was assessed with a variety of different compounds since environmental or occupational exposures to chemicals usually occur in combination with other chemicals. Pozzani et al. (1959) determined that 1,2-dichloropropane has an additive toxic effect (LD_{50} assessed) when given orally or by inhalation to rats with 1,1,2-trichloroethane, and when given with both ethylene dichloride and perchloroethylene. Drew et al. (1978) reported that inhalation of 1,2-dichloropropane in combination with trichloropropane by rats did not result in a greater-than-additive toxic effect (serum enzymes assessed: SGOT, SGPT, G-6-phosphatase, ornithine carbamyl transferase). Tsulaya et al. (1979) and Sidorenko et al. (1976, 1979) determined that inhalation of 1,2-dichloropropane has an additive effect in rats and mice when given in combination with 1,2,3-trichloropropane and perchloroethylene (effects on lung, liver and nervous system assessed).

2.8 POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE

No populations with unusual or increased susceptibility to the health effects of 1,2-dichloropropane could be identified based on the available literature.

2.9 ADEQUACY OF THE DATABASE

Section 104 (i) (5) of CERCLA, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of 1,2-dichloropropane is available. Where adequate information is not available, ATSDR, in cooperation with the National Toxicology Program (NTP), is required to assure the initiation of a program of research designed to determine these health effects (and techniques for developing methods to determine such health effects). The following discussion highlights the availability, or absence, of exposure and toxicity information applicable to human health assessment. A statement of the relevance of identified data needs is also included. In a separate effort, ATSDR, in collaboration with NTP and EPA, will prioritize data needs across chemicals that have been profiled.

2.9.1 Existing Information on the Health Effects of 1,2-Dichloropropane

The existing data on health effects of inhalation, oral, and dermal exposure of humans and animals to 1,2-dichloropropane are summarized in Figure 2-5.

Data regarding the toxic effects of 1,2-dichloropropane on humans result solely from case reports of people exposed by inhalation, ingestion or skin exposure. The case reports contain information regarding the lethal and systemic effects of acute inhalation and oral exposure to the agent. These reports indicate that 1,2-dichloropropane primarily affected the central nervous system, liver, and kidneys, but respiratory and hematopoietic system alterations were also observed. Chronic dermal exposure to 1,2-dichloropropane in aerosol form in the workplace resulted in dermatitis.

There are data regarding the lethality and toxic effects of 1,2-dichloropropane in animals exposed by inhalation for acute and intermediate time periods. The central nervous system, respiratory system, liver, and kidney are the major target organs of 1,2-dichloropropane toxicity. Hematological effects are also reported. A limited study on the carcinogenicity of 1,2-dichloropropane in mice after inhalation exposure has been done and has suggested that 1,2-dichloropropane was carcinogenic (see Section 2.2.1.8), but the study is unreliable (high mortality occurred in the exposed group; tumor incidence in controls was not reported; morphology of the hepatomas was inadequately characterized) so no conclusions may be drawn.

Data are available regarding the lethality and toxic effects of 1,2-dichloropropane in animals orally exposed for acute, intermediate and chronic time periods. These data show that the liver is the main target organ for the toxic effects of 1,2-dichloropropane; effects on the hematological and nervous systems were also observed. An increase in the incidence of a developmental effect in rats (delayed ossification of the bones of the skull) was also observed. The carcinogenicity in rats and mice after chronic oral exposure to 1,2-dichloropropane was assessed and carcinogenic potential was found in both species: there was equivocal evidence in female rats (chemically related marginal increase in adenocarcinomas of the mammary gland), no evidence in male rats (no chemically related increases in neoplasms), and some evidence in male and female mice (chemically increased incidence of hepatocellular neoplasms).

Application of 1,2-dichloropropane to the skin or eye of rabbits produced irritation. Application to the skin of rabbits has also produced death.

No genotoxic effects were found in a dominant-lethal study in rats.

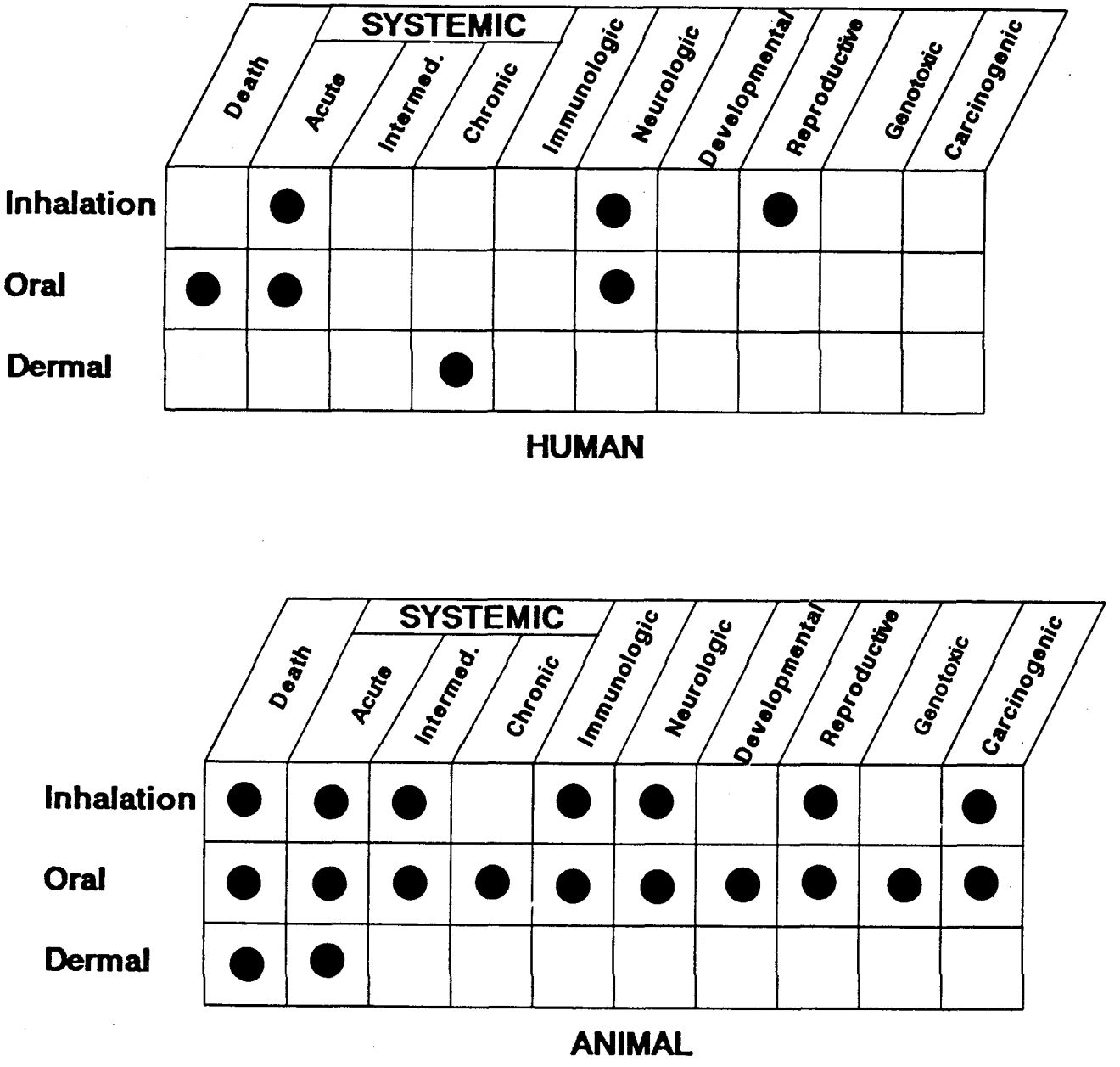


FIGURE 2-5. Existing Information on Health Effects of 1,2-Dichloropropane

Genotoxicity data in bacteria, fungus, Drosophila and mammalian cell lines was evaluated. The preponderance of data indicate that 1,2-dichloropropane ,is mutagenic in these systems.

2.9.2 Data Needs

Single Dose Exposure. Information regarding single inhalation and oral exposure of various animal species to 1,2-dichloropropane provides information on lethal effect levels. The limited data available on the non-lethal effects of a single dose of 1,2-dichloropropane show effects on the liver and kidney. More studies that use non-lethal doses and examine tissues histologically might provide information on dose-response relationships and mechanisms of lethality and toxicity. Single dose dermal and ocular studies in rabbits have shown that 1,2-dichloropropane is a skin and eye irritant. Additional observations in other species of animals dermally exposed to 1,2-dichloropropane would help to more fully characterize the irritative effects of this chemical.

Repeated Dose Exposure. Available repeated exposure inhalation and oral studies of 1,2-dichloropropane provide information on the lethal and non-lethal effects in various species of animals. The major target organs for the effects of 1,2-dichloropropane are the central nervous system, liver and kidney, and effects on the respiratory, hematological systems and body weight were also seen. Repeated dose dermal studies with animals are not available but would provide information on the possible systemic effects of 1,2-dichloropropane. Since occupational dermal exposure has resulted in dermatitis in humans, repeated dermal dose studies in animals might also provide information on allergic responses as well as local irritation.

Chronic Exposure and Carcinogenicity. Well-conducted chronic oral gavage studies provide information on the systemic and carcinogenic effects of 1,2-dichloropropane in rats and mice. Chronic inhalation, oral drinking water, and dermal animal studies are not available but could provide information on similarity of systemic effects across routes and dose-response data that may be useful for human health risk evaluation. These studies may also help categorize the carcinogenic potential of 1,2-dichloropropane in humans.

Genotoxicity. The available genotoxicity studies conducted with bacteria, fungus, and mammalian cell lines indicate that 1,2-dichloropropane is genotoxic in some systems. A dominant-lethal study in rats resulted in no genotoxic effects, but further in vivo studies with mammals will help fully characterize the genotoxic potential of 1,2-dichloropropane, with regard to potential for heritable mutations, chromosomal damage, and chromosomal aberrations. Cell transformation studies may also be useful to augment carcinogenesis bioassays.

Reproductive Toxicity. Histological examination of the reproductive organs of female rats and mice exposed orally to 1,2-dichloropropane for subchronic or chronic durations, showed inflammation of the uterus and ovary and hyperplasia of the mammary gland. It was not found conclusively that these effects were compound-related; this uncertainty and the fact that limited human data (metrorrhagia) suggest an adverse effect on the reproductive system suggests that additional studies examining the effects of 1,2-dichloropropane on the female reproductive organs are desirable. Male and female reproductive organs in rodents were also histologically examined after subchronic and chronic oral exposure but no compound-related lesions were found. A 2-generation oral reproduction study is now in progress, and the results of these studies will provide further information regarding any reproductive effects of 1,2-dichloropropane in animals, which then may be related to possible reproductive effects in humans. Studies examining the reproductive effects of 1,2 dichloropropane following inhalation and dermal exposure of animals would also be helpful in assessing the potential effects in humans.

Developmental Toxicity. Toxic effects in rats (delayed ossification of the bones of the skull) have been found following oral exposure to 1,2-dichloropropane. Further studies using a greater range of doses and studies testing other relevant routes of exposure would provide information on possible fetotoxic and teratogenic effects in animals that might be relevant to humans.

Immunotoxicity. Subchronic and chronic oral studies in rats and mice have found no adverse effects after histological examination of organs and tissues of the immunological system, but a battery of immunotoxicity tests have not been performed. A decrease in thymus weight and a decrease in cortical lymphoid cells were found in mice following acute inhalation exposure to 1,2-dichloropropane, but no tests of immunological function were performed. These studies in animals by relevant environmental routes would provide a better assessment of immunotoxic effects than histological examination of organs and tissues. Two case studies suggested that 1,2-dichloropropane may sensitize humans. Testing in animals to determine the dose and time of exposure needed to sensitize animals would be helpful in determining levels of 1,2-dichloropropane leading to sensitization in , humans.

Neurotoxicity. Signs of central nervous system toxicity have been seen in humans after both inhalation and oral exposure. Signs of central nervous system toxicity were found in animals acutely exposed to 1,2-dichloropropane by inhalation and in animals treated orally with 1,2-dichloropropane (acute and subchronic exposures). Functional Observational Batteries have been performed on rats acutely exposed to 1,2-dichloropropane and neurological effects (decrease in activity) were found at ≥300 mg/kg/day. A battery of tests by other relevant routes of exposure and the assessment of neuropathology using specialized fixation methods would provide further

information on the neurotoxicity in animals, which may relate to possible neurotoxic effects in humans.

Epidemiological and Human Dosimetry Studies. In humans, 1,2-dichloropropane primarily affects the central nervous system, liver and kidney. This information comes from case studies where patients either inhaled or ingested 1,2-dichloropropane, accidentally or as a suicide attempt. The only occupational exposure was reported in a Polish study in which two women out of sixty that were dermally exposed to liquid 1,2-dichloropropane developed allergic dermatitis. The most likely routes of exposure for the United States general population are through inhalation of contaminated ambient air or consumption of contaminated drinking water. As discussed in Chapter 5, the use of 1,2-dichloropropane as a consumer solvent and as a soil fumigant has been discontinued. 1,2-Dichloropropane is now used as a commercial solvent, but only in closed systems. Therefore, exposure to the general population via inhalation should be much lower than in the past. The most likely exposure to humans is the consumption of contaminated drinking water resulting from the use of 1,2-dicholopropane soil fumigant in agricultural areas. Elimination of 1,2-dichloropropane from the groundwater is slow so that contamination may remain for a long and indeterminate period of time. The monitoring of urine and blood levels of 1,2-dichloropropane in populations exposed to contaminated drinking water or air (such as those living near industries using 1,2-dichloropropane as a solvent, those living near hazardous waste sites, or those people occupationally exposed) and the correlation of these levels with health effects, may provide a basis for further epidemiological studies.

Biomarkers of Disease. Secchi and Alessio (1968, 1971) reported differences in hepatic enzymes found in human serum as an indicator of hepatic damage resulting from ingestion of 1,2-dichloropropane. It was found that cytoplasmic liver enzymes found in the serum indicated less severe damage to hepatocytes, while mitochondrial and lysosomal liver enzymes found in the serum indicated severe liver damage, which usually results in death. Further epidemiological studies may validate these indices and correlate other parameters with a particular disease state resulting from exposure to 1,2-dichloropropane.

Disease Registries. At present, the only toxicological effects of 1,2-dichloropropane reported in humans are acute effects resulting from ingestion or inhalation of cleaning solvents containing 1,2-dichloropropane. If epidemiological studies identify particular diseases associated with 1,2-dichloropropane exposure, it may be possible to determine the number of people affected and the factors associated with identifying the disease in certain populations, such as exposure to 1,2-dichloropropane in the ambient air or in the drinking water near hazardous waste sites.

Bioavailability from Environmental Media. Detection of exposure to 1,2-dichloropropane through urinalysis, blood analysis, and odor thresholds have been studied (Amoore and Hautala 1983, Ghittori et al. 1987, Cramer et

al. 1988). Epidemiology studies that correlate levels of 1,2-dichloropropane in the environment with levels in human tissues, blood or urine and with specific health effects would be useful. While no data on the uptake of 1,2-dichloropropane in other tissue or bodily fluids are available, a pilot study demonstrated that similar low molecular weight chlorinated alkanes are found in human milk (Pellizzarri et al. 1982). The source of these pollutants was probably ambient air. The major source of human exposure to 1,2-dichloropropane could be from contaminated well water, and an animal study (Hutson et al. 1971) indicates that it is readily adsorbed from the GI tract. An analysis of body fluids of those people whose drinking water contains 1,2-dichloropropane or who have come into contact (orally or dermally) with soil contaminated with 1,2-dichloropropane, may allow a determination of the existence of exposure and bioavailability of the chemical.

Food Chain Bioaccumulation. 1,2-Dichloropropane has not been reported in food or biota nor were any studies located in which the uptake of this chemical in plants or animals was investigated. The bioaccumulation potential for a chemical is most conveniently studied by measuring the bioconcentration factor (BCF) or the concentration of a chemical in fish divided by the concentration in water from which the chemical is taken up. Lacking any data on such studies for 1,2-dichloropropane, the bioaccumulation can be estimated from its partitioning behavior between octanol and water which, in turn, can be estimated from structure-activity relationships. Accordingly, the BCF of 1,2-dichloropropane estimated from its K,, is 18 (Lyman et al. 1982, Eqn 5-2), indicating that there is a very low potential for bioaccumulation in the food chain.

Absorption, Distribution, Metabolism, Excretion. The only in vivo toxicokinetic data of 1,2-dichloropropane are the inhalation metabolism and the excretion study of Timchalk et al. (1989), oral metabolism and excretion studies of Hutson et al. (1971) and Timchalk et al. (1989), the oral metabolism study of Jones and Gibson (1980), and the intraperitoneal excretion study of Trevisan et al. (1988). These studies indicate that inhaled 1,2-dichloropropane and orally administered 1,2-dichloropropane are readily and extensively absorbed by the gastrointestinal tract, is primarily metabolized to N-acetyl-S-(2-hydroxypropyl)cysteine, and is rapidly excreted in the urine, feces and expired air. Studies in animals of the rate and extent of absorption and distribution following exposure to all three routes, and metabolism and excretion following dermal exposure would provide more complete characterization the pharmacokinetics of 1,2-dichloropropane, Ghittori et al. (1987) and Cramer et al. (1988) reported methods for detection of 1,2-dichloropropane in urine and blood. These methods may provide means of monitoring human exposure and of extrapolating results from animal studies,

Comparative Toxicokinetics. No studies were found that evaluated differences in toxicokinetics between species. Toxicokinetic differences may explain the increased sensitivity of mice to the toxic effects of 1,2-

dichloropropane in comparison to other species. Ethical considerations limit the amount of information that can be obtained in humans, but analysis of the urine of people with known exposure to the parent compound or its metabolites could provide knowledge of the metabolic 'pathways in humans. Qualitative and quantitative comparison of human metabolites with those of animals could help identify the most appropriate species to serve as a model for predicting toxic effects in humans and studying the mechanisms of action.

2.9.3 On-going Studies

The EPA (1987d) issued a final rule requiring the manufacturers and processors of 1,2-dichloropropane to conduct health effects studies. All of the required studies have been incorporated into this profile, except for a 2-generation oral study, which has yet to be completed.

3. CHEMICAL AND PHYSICAL INFORMATION

3.1 CHEMICAL IDENTITY

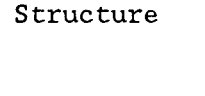
Data pertaining to the chemical identity of 1,2-dichloropropane are listed in Table 3-l.

3.2 PHYSICAL AND CHEMICAL PROPERTIES

The physical and chemical properties of 1,2-dichloropropane are presented in Table 3-2.

3. CHEMICAL AND PHYSICAL INFORMATION

TABLE 3-1. Chemical Identity of 1,2-Dichloropropane

	Value	References
Chemical name	1,2-Dichloropropane	CAS 1988
Synonyms	Propylene dichloride; propylene chloride; 2,3-dichloropropane; 1,2-D	CAS 1988, SANSS 1988; Cohen 1986
Trade name(s)[a]	D-D Mixture; Nemex; Vidden D; D-D; Dow-421; Terr-o-gas; Dowfume NC; Vorlex; EP-201; D-D Pilfume; Terr-o-cide; New Fieldfume; Dorlone	Bennett 1981, 1982, 1983; OHM-TADS 1988; Ali et al. 1986; HSDB 1988; EPA 1979
Chemical formula	$C_3H_6Cl_2$	CAS 1988
Chemical Structure		SANSS 1988
Identification Numbers:		
CAS Registry	78-87-5	CAS 1988
NIOSH RTECS	TX9625000	RTECS 1988
EPA Hazardous Waste	U083	EPA 1982
OHM-TADS	7216876	OHM-TADS 1988
DOT/UN/NA/IMCO Shipping	Propylene dichloride; UN 1279; IMCO 3.2	OHM-TADS 1988
HSDB	1102	HSDB 1988
NCI	C55141	HSDB 1988

[a]Includes names of those products which contain 1,2-dichloropropane in a mixture of compounds.
CAS = Chemical Abstracts Service
NIOSH = National Institute for Occupational Safety and Health
RTECS = Registry of Toxic Effects of Chemical Substances
OHM-TADS = Oil and Hazardous Materials/Technical Assistance Data System
DOT/UN/NA/IMCO = Department of Transportation/ United Nations/ North/America/International Maritime Dangerous Goods Code
HSDB = Hazardous Substances Data Bank by the National Library of Medicine
NCI = National Cancer Institute

TABLE 3-2. Physical and Chemical Properties of 1,2-Dichloropropane

Property	Value	Reference
Molecular weight	112.99	Riddick et al. 1986
Color	Colorless	Hawley 1981
Physical state	Liquid	Riddick et al. 1986
Freezing point	-100.44°C	Riddick et al. 1986
Boiling point	96.37°C	Riddick et al. 1986
Density, 20°C	1.15597	Riddick et al. 1986
Odor	Chloroform-like	Hawley 1981
Odor threshold		
Water	0.010 ppm (w/v)	Amoore and Hautala 1983
Air	0.25 ppm (v/v)	Amoore and Hautala 1983
Solubility		
Water	2,700 mg/L (20°C)	Horvath 1982
Organic solvents	Miscible with most common solvents	Hawley 1981
Partition coefficients		
Log octanol/water	1.99 (estimated)	EPA 1988b
Log K_{oc}	1.67[a]	Chiou et al. 1979
Vapor pressure	49.67 mm Hg (25°C)	Riddick et al. 1986
Henry's Law constant	2.07×10^{-3} atm-m^3/mol (24°C)	Mackay and Yeun 1983
	1.67×10^{-3} atm-m^3/mol (24°C)	Chiou et al. 1980
Autoignition temperature	557°C	Parrish 1983
Flash point, closed cup	16°C	Parrish 1983

TABLE 3-2 (continued)

Property	Value	Reference
Flammability limits	3.4 to 14.5 vol %	Parrish 1983
Conversion factors mg/m^3 to ppm (v/v) in air (20°C)	1 mg/m^3 = 0.21 ppm (v/v)	

[a]Using $K_{oc} = 1.724\ K_{om}$

4. PRODUCTION, IMPORT, USE AND DISPOSAL

4.1 PRODUCTION

1,2-Dichloropropane is produced by Columbia Organics in Cassatt, SC, Dow Chemical in Freeport, TX and Dow Chemical in Plaquemine, LA (SRI 1988; USITC 1987); however, Dow Chemical Company is the only manufacturer of the isolated chemical in the United States (EPA 1986c). The total output of 1,2-dichloropropane by U.S. manufacturers remained relatively stable until 1984 when a major manufacturer, Mannsville Chemical Products Corporation, discontinued production (IARC 1986). The domestic production volume of 1,2-dichloropropane during 1984 was 59.8 million pounds (IARC 1986). Over 95% of the approximately 75 million pounds produced in 1982 was used on site as a captive chemical intermediate in the production of perchloroethylene and other chlorinated products (EPA 1986c, Dow Chem. Co. 1983). High-purity 1,2-dichloropropane, marketed as a solvent, is obtained as a by-product of the synthesis of propylene oxide by the chlorohydrin process. The high-purity product may also be obtained by the reaction of propylene and chlorine in the presence of an iron oxide catalyst at moderate temperature (45°C) and pressure (25-30 psia). Pesticide products that contain 1,2-dichloropropane were distillates of the chlorination of propylene (IARC 1986). However, Dow discontinued production of 1,2-dichloropropane for agricultural use, and pesticidal formulations containing this chemical, such as D-D, are unavailable in the U.S. (Meister 1987). By 1983, 1,2-dichloropropane was no longer sold for consumer use in paint strippers, paint varnish, and furniture finish removers (EPA 1986c; Dow Chem. Co. 1983). This indicates that production for sale, as opposed to internal consumption by manufacturers, has been greatly curtailed in the early 1980s.

4.2 IMPORT

Mobay Corporation imported 1 million lbs of 1,2-dichloropropane from the German Federal Republic in 1986 (EPA 1987c). Mobay currently imports 1,2-dichloropropane from the German Federal Republic on an as-need basis on customer's request, Other data pertaining to the import of 1,2-dichloropropane were not located in available literature.

4.3 USE

Based on 1982 production data supplied by Dow (EPA 1986c), it has been estimated that over 95% of the isolated product manufactured by Dow Chemical is used on-site as a captive intermediate in the production of perchloroethylene and other chlorinated products by their 'per-tet' process (EPA 1986c, Dow Chem. Co. 1983). Approximately 3 million pounds per year of dichloropropane was marketed by Dow Chemical in 1982 for use as an industrial solvent for oils, fats, resins, waxes, and rubber, in ion exchange manufacture, in toluene diisocyanate (TDI) production, in photographic film manufacture, for paper coating, and for petroleum catalyst regeneration (HSDB 1988; IARC 1986; EPA 1986c). As of 1982, Dow Chemical no

longer sold 1,2-dichloropropane for use as a solvent in paint strippers, paint, varnish, and furniture finish removers as a low-cost alternative to methylene chloride. It had been a component of 10 of,these products (EPA 1986c). By the end of 1983, its use as a solvent for film production was to be phased out in favor of l,l,l-trichloroethane (Dow 1983). According to Dow (1989), the phaseout of use of 1,2-dichloropropane as a solvent for film production had not occurred as of June, 1989, although it is still planned. They further stated that the use of 34% in TDI production has now been discontinued, Outside of its use as a chemical intermediate, Dow Chemical Company's use pattern for 1,2-dichloropropane in 1982 was 41% in ion exchange manufacturing, 34% in toluene diisocyanate (TDI) production, 19% in photographic film production, 4% in paper coating, and 2% in petroleum catalyst regeneration (Dow 1983).

An estimated 20 million pounds/year of dichloropropane were produced as a by-product in a mixture marketed as a soil fumigant which had been used in the cultivation of a variety of crops, including citrus fruits, pineapple, soya beans, cotton, tomatoes, and potatoes (IARC 1986; HSDB 1988). Dow has discontinued production of soil fumigants containing 1,2-dichloropropane, and pesticidal formulations containing this chemical are no longer available in the U.S. (Meister 1987). Other uses for 1,2-dichloropropane include an intermediate in the synthesis of carbon tetrachloride, lead scavenger in gasoline, textile stain remover, oil and paraffin extractant, scouring compound, and metal degreasing agent, especially prior to electroplating (IARC 1986). However, the largest manufacturer of 1,2-dichloropropane, Dow Chemical Co. (1989), is not aware of its current uses as a lead scavenger in gasoline, textiles, stain remover, oil and paraffin extractant, scouring compound, and metal degreasing agent.

4.4 DISPOSAL

Incineration under controlled conditions appears to be the most viable method of disposal for 1,2-dichloropropane (OHM-TADS 1988; HSDB 1988). It is reported that Dow Chemical incinerates 7 million pounds of 1,2-dichloropropane annually (EPA 1986c). Disposal through the use of a liquid injection incinerator requires a temperature range of 650 to 1600°C and residence time of 0.1 to 2 seconds. A rotary kiln incinerator requires a temperature range of 820 to 1600°C and a residence time of seconds. A fluidized bed incinerator requires a temperature range of 450 to 980°C and a residence time of seconds (HSDB 1988). Where land disposal of waste residue containing 1,2-dichloropropane is sought, environmental regulatory agencies should be consulted on acceptable disposal practices (HSDB 1988). 1,2-Dichloropropane may also be a constituent of wastewater streams where it would be susceptible to removal by air stripping (EPA 1986c).

4.5 ADEQUACY OF THE DATABASE

Section 104 (i) (5) of CERCLA, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the

Public Health Service) to assess whether adequate information on the health effects of 1,2-dichloropropane is available. Where adequate information is not available, ATSDR, in cooperation with the National Toxicology Program (NTP), is required to assure the initiation of a program of research designed to determine these health effects (and techniques for developing methods to determine such health effects). The following discussion highlights the availability, or absence, of exposure and toxicity information applicable to human health assessment. A statement of the relevance of identified data needs is also included. In a separate effort, ATSDR, in collaboration with NTP and EPA, will prioritize data needs across chemicals that have been profiled.

4.5.1 Data Needs

Production, Import, Use, and Disposal. Production methods for 1,2-dichloropropane are described in the literature. While former major uses of 1,2-dichloropropane are known, there has been a phasing out of many of the applications with the greatest potential for population exposure. Current information concerning production volume and use is lacking. This type of information is absolutely necessary for estimating the potential for environmental releases from various industries, as well as potential concentrations in the environmental. Knowledge of what consumer products contain 1,2-dichloropropane is essential for estimating general population exposure. Unfortunately, this type of information is difficult to obtain in detail since companies consider it to be confidential business information. According to the Emergency Planning and Community Right to Know Act of 1986 (EPCRTKA), (§313), (Pub. L. 99-499, Title III, §313), industries are required to submit release information to the EPA. The Toxic Release Inventory (TRI), which contains release information for 1987, became available in May of 1989. This database will be updated yearly and should provide a more reliable estimate of industrial production and emission.

5. POTENTIAL FOR IITJMAN EXPOSURE

5.1 OVERVIEW

1,2-Dichloropropane is a man-made chemical whose presence in the environment results from anthropogenic activity. Emission sources of 1,2-dichloropropane include process and fugitive emissions from its production and use as a chemical intermediate and industrial solvent, and evaporation from wastewater streams. Many of the major uses of 1,2-dichloropropane, other than as a chemical intermediate and industrial solvent, have been eliminated or curtailed. Most importantly, all uses with significant consumer and general population exposure may have been eliminated in the U.S. 1,2-Dichloropropane is no longer used as a soil fumigant in the United States, a use that has been responsible for polluting groundwater supplies in some agricultural areas. Its major producer, Dow Chemical Company, has recommended that it no longer be used in paint stripping formulations, varnish, and furniture finish removers, uses with potential for widespread consumer and occupational exposure. Dow Chemical Company asserts that occupational exposure is minimal since all their processes involving the production, conversion, or disposal of 1,2-dichloropropane are in closed systems. Additionally, vent gas from their production process is destroyed by thermal oxidation. There is evidence that there were substantial releases of 1,2-dichloropropane into wastewater by industries that use 1,2-dichloropropane as a solvent. An example of such industries are those that use 1,2-dichloropropane in the manufacture of ion exchange resins.

The major releases of 1,2-dichloropropane will be to the atmosphere and to soil. However, when 1,2-dichloropropane is spilled on soil, landfilled, or applied to soil, as it formerly had been, as a fumigant, it will partially volatilize, and the remainder will leach into the subsurface soil and groundwater. In one experiment in which soil was treated with 1,2-dichloropropane, immediately covered with 12 cm of untreated soil and stored outdoors in open jars protected from rain, 99% of the chemical was lost within 10 days. With the elimination of 1,2-dichloropropane's use in agriculture, its potential for polluting groundwater has been substantially reduced. In groundwater, where volatilization is unlikely, the principal reactions will be hydrolysis and anaerobic biotransformation. Hydrolysis is estimated to be very slow (half-life 25-200 weeks) and the potential for anaerobic biotransformation has not been evaluated. Therefore groundwater supplies that are contaminated with 1,2-dichloropropane may remain so for a long and indeterminate period of time.

The dominant removal process of 1,2-dichloropropane in the atmosphere is expected to be reaction with photochemically-generated hydroxyl radicals (half-life >23 days). Washout in precipitation should also occur; although most 1,2-dichloropropane removed by this mechanism is likely to reenter the atmosphere by volatilization. Since degradation in the atmosphere is slow, considerable dispersion of 1,2-dichloropropane from source areas can occur before it degrades or is removed in washout. Besides dispersal, importation

of 1,2-dichloropropane may also occur from other countries where it may be more widely used. Volatilization will be the primary fate process in surface water (half-life 5.8 hr in a model river). In soil, 1,2-dichloropropane is expected to volatilize rapidly from the soil surface and. to leach into the ground, where the potential for groundwater contamination exists.

The general population may be exposed to low levels of 1,2-dichloropropane through inhalation of contaminated ambient air, consumption of contaminated drinking water, or dermal contact. With the elimination of its use as a soil fumigant and curtailment of its use in paint strippers, varnishes, and furniture finish removers, exposure of the general population to 1,2-dichloropropane by inhalation or dermal contact should be much lower than it once was. Any groundwater supplies that are already contaminated, may remain so for a long time. A 1981-1983 National Occupational Exposure Survey (NOES) by NIOSH estimated that 2119 non-agricultural workers, including 949 females, were potentially exposed to 1,2-dichloropropane in the United States. The number of exposed workers should be much lower now because of the chemical's diminished use. Occupational exposure is primarily by inhalation and dermal contact,

5.2 RELEASES TO THE ENVIRONMENT

5.2.1 Air

The total estimated annual environmental release of 1,2-dichloropropane from production and industrial use, primarily in the manufacture of perchloroethylene, was 1,146,OOO lbs (EPA 1986c). This figure represents releases regulated by the Toxic Substances Control Act (TSCA), and therefore excludes pesticidal uses of 1,2-dichloropropane. Of these releases, 772,000 lbs were to air, 198,000 lbs to water, and 176,000 lbs to land disposal sites. They include releases from process emissions to the air, secondary air emissions resulting from volatilization during wastewater treatment (aeration), releases to water in wastewater effluent, emissions to air from incomplete incineration, and land disposal of solid waste residues. The inclusion of fugitive emissions would increase the total. Recently it has been shown that a variety of chlorinated organic compounds are formed during combustion of hydrocarbons when chlorine is present; two isomers of dichloropropane were among the more than 100 chemicals formed during the combustion of propane in the presence of HCl under oxygen deficient conditions (Eklund et al. 1987). These conditions may occur in municipal incinerators and, therefore, 1,2-dichloropropane may be released from incinerators. A correlation of data from the EPA Air Toxics Emission Inventory with industrial source categories (SIC codes), shows volatile emissions of 1,2-dichloropropane from electronic components, photographic equipment and supplies, and apartment building operators (SIC Codes 3679, 3861, 6513). (EPA 1987a).

5. POTENTIAL FOR HUMAN EXPOSURE

5.2.2 Water

The total estimated annual environmental re1eas.e of 1,2-dichloropropane in wastewater from production and industrial use was 198,000 lbs (EPA 1986c). Table 5-l shows the types of industries that discharged 1,2-dichloropropane, their frequency of release, and concentrations in wastewater. These data come from a comprehensive wastewater survey conducted by EPA's Effluent Guidelines Division. Over 4000 samples of wastewater from a broad range of industrial facilities and publicly-owned treatment works were analyzed in this survey. Between 1980 and 1988, 708 samples of wastewater in EPA's STORET database were analyzed for 1,2-dichloropropane (STORET 1988). Ten percent of the samples were 10 parts per billion (ppb) or higher with a maximum level of 910 ppb. Unfortunately, the detection limit is apparently recorded when no chemical is detected, so it is impossible to say whether the 90 percentile figure represents positive samples or merely higher detection limits.

1,2-Dichloropropane was found at concentrations of 5.6, 22, 60, 310 ppb in four outfalls from the Dow Chemical of Canada plant into the St. Clair River for a net loading of 11.8 kg/day (King and Sherbin 1986). This survey was performed as a result of puddles of chlorinated hydrocarbons discovered on the bottom of the St. Clair River. These chemicals are thought to be products or byproducts of chlorinated hydrocarbon manufactured at this site. Waste from this operation is now being incinerated but was historically landfilled. Landfill leachate from the landfill is treated with carbon and then discharged. The concentration of 1,2-dichloropropane before and after treatment was 320 and 510 ppb. However, the carbon filter was reportedly spent at the time of the survey.

Rohm and Haas in Philadelphia, PA, a manufacturer of ion exchange resins, discharged weekly average amounts of 1,2-dichloropropane of 60-2250 lbs/day into the Northeast Philadelphia Treatment Plant during August and September of 1981 (Hinnegan 1981). The daily amount of 1,2-dichloropropane discharged on five days in 1979 ranged from 37.2 to 5100 lbs (Weston 1980). The report covering the discharges in 1979 stated that on 4 days Rohm and Haas contributed all of the 1,2-dichloropropane influent going into Philadelphia's Northeast Water Pollution Control Plant (NEWPCP). On one day, 35% came from elsewhere. At times, all of the 1,2-dichloropropane was removed in the treatment plant. Tidal excursions of the NEWPCP effluents affects the intake of the Baxter Drinking Water Plant, located 2 miles upstream on the Delaware River. EPA's Philadelphia Geographic Area Pollutant Survey found that average 1,2-dichloropropane concentration in the intake water during 1982-1983 was 1.6 ppb, indicating that 1,2-dichloropropane was being discharged from the wastewater treatment plant into the Delaware River (EPA 1986~). If the typical daily discharge from the Rohm and Haas plant was 500 lbs, then the annual discharge would have been 182,000 lbs, a figure approaching the estimated 198,000 lbs of 1,2-dichloropropane discharged into waterways for all production and industrial use. It is not clear for what year the estimated environmental release

TABLE 5-1. Sources of of 1,2-Dichloropropane Effluents[a]

Industry	Frequency	Concentration (ppb)		
		Maximum	Medium	Low
Paint and ink	3	3457.22	38.9176	29.30
Organics and plastics	2	15.93	38.92	6.25
Inorganic chemicals	14	54.30	3.31	0.74
Textile mills	2[b]	40.43	38.76	37.09
Plastics and synthetics	1	5.60	5.60	5.60
Rubber processing	1	0.82	0.82	0.82
Auto and other laundries	1	66.92	66.92	66.92
Pesticides manufacture	1	0.90	0.90	0.90
Photographic industries	3	121.79	36.34	3.59
Organic chemicals	16	1411.98	23.67	1.23
Publicly owned treatment works	4	52.22	24.86	1.94
Industry unknown	4	60.03	27.07	22.44

[a]Source: Shackelford et al. 1983.
[b]Incorrectly listed as 1 in reference; data are consistent with a frequency of 2.

figure applies and whether the releases into water include industrial discharges that may undergo treatment before being discharged into a waterway or only that which is discharged into a waterway. As of January, 1989, Rohm and Haas has discontinued use of 1,2-dichloropropane in the manufacture of ion exchange resins (Rohm and Haas 1989). There are three' other manufacturers of ion exchange resins in the U.S. with potentially similar release patterns (HSDB 1988). 1,2-Dichloropropane was only detected in one sample at 3 ppb from Eugene, OR in the National Urban Runoff Program which analyzed runoff in 86 samples from 19 cities throughout the U.S. (Cole et al. 1984).

5.2.3 Soil

The total estimated annual environmental release of 1,2-dichloropropane by industry into land disposal sites was 176,000 lbs (EPA 1986c). This is not the recommended method of disposal and this figure may have been much higher in the past.

In the past, the major source of release of 1,2-dichloropropane into soil was from its use as a soil fumigant for nematodes. For this purpose, the fumigant was injected into the root zone, after which the soil was compacted to enhance retention of the vapor. However, 1,2-dichloropropane is no longer permitted to be used in the U.S. for agricultural purposes because this use pollutes groundwater.

Production of 1,2-dichloropropane for use as a solvent in consumer products such as paint strippers, varnishes, and furniture finish removers, from which inadvertent releases to soil (i.e. spills) would be expected, has been discontinued. In addition to spills, chemicals can be released into soil from leaking storage tanks. A case of groundwater contamination by 1,2-dichloropropane resulting from a leaking underground storage tank at a paint factory has been documented in the literature (Botta et al. 1984).

Releases into the subsoil and groundwater can also result from the landfilling of process residues. Four out of 11 samples of landfill leachate in Minnesota and Wisconsin contained 2.0-81 ppb 1,2-dichloropropane (Sabel and Clark 1984).

5.3 ENVIRONMENTAL FATE

5.3.1 Transport and Partitioning

The relatively high water solubility of 1,2-dichloropropane suggests that washout by rain should be an important process for removing the chemical from the atmosphere. The dominant removal process for 1,2-dichloropropane from surface waters is expected to be volatilization. Based on the measured relative mass transfer coefficient of 1,2-dichloropropane between water and air of 0.57 (Cadena et al. 1984) and the range of reaeration coefficients typical of relatively rapid and shallow streams

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found in the western U.S., 0.14 to 1.96 hr-1 (Cadena et al. 1984), the half-life of 1,2-dichloropropane in these streams will range from 0.62 to 8.68 hr. The residence time in a lake or pond would be much longer. Based on measured Henry's Law Constant at 24°C of $1.67x10^{-3}$ atm-m^3/mol (Chiou et al. 1980) and $2.07x10^{-3}$ atm-m^3/mol (Mackay and Yeun 1983), the volatilization half-life of 1,2-dichloropropane in a model river 1 m deep flowing 1 m/sec with a wind speed of 3 m/sec is estimated to be 3.7-4.6 hr, with resistance in the liquid phase controlling volatilization (Lyman et al. 1982). In such cases, the current will have a much greater effect on volatilization than the wind speed. In wastewater treatment plants that receive volatile compounds such as 1,2-dichloropropane from industrial discharges or other sources, stripping will be an important mechanism for transferring the chemical from the water into the air. In stripping, as opposed to ordinary volatilization, the liquid and gas phases are dispersed with the result that the interfacial surface area is much greater and liquid/gas mass transfer is greatly enhanced. More than 99% removal of 1,2-dichloropropane from wastewater plants has been attributed to this process (Kincannon et al. 1983).

The K_{oc} of 1,2-dichloropropane is 47 in a silt loam soil (Chiou et al. 1979). This value is low, suggesting that 1,2-dichloropropane will not adsorb appreciably to soil, sediment, and suspended solids in water. 1,2-Dichloropropane sorbs to clay minerals in dry soil but desorbs when the soil is moist (Cohen et al 1984). Where 1,2-dichloropropane has been used as a soil fumigant for nematodes in California and the coastal areas of Georgia, South Carolina, North Carolina, and Virginia, the soils are sandy and have a low organic carbon content (Cohen et al. 1984). Adsorption to these soils will be lower than to soils with a higher organic content and should not reduce the mobility of 1,2-dichloropropane significantly. The leaching potential of 1,2-dichloropropane is illustrated by a case study in California in which a soil core was taken from an agricultural field where a fumigant containing the chemical had recently been used. Residues of 1,2-dichloropropane up to 12.2 ppb were detected throughout much of the 24-foot core profile and two adjacent drinking water wells contained concentrations of 1,2-dichloropropane in excess of 10 ppb (Ali et al. 1986). As much as 300 ppt of 1,2-dichloropropane have been detected in bank-filtered Rhine River water indicating that all of the chemical was not being retained by the soil (Piet and Morra 1979). The finding that highly mobile and biologically-resistant residues of the fumigant pesticide 1,2-dibromoethane persisted in topsoil for years after application, despite its mobility and volatility, spurred a study of this phenomenon in other halogenated hydrocarbons (Sawhney et al. 1988). Sandy loam soils treated with 10,000 ppm of 1,2-dichloropropane for 1 day were extracted 16 times with water. The apparent soil water partition coefficient, initially 0.56 (K_{oc} 22), rose to 72 (K_{oc} 2800); the final concentration of 1,2-dichloropropane in the soil was 1.4 ppm . After a 57-day period, the apparent partition coefficient was >250 (K_{oc} >9700). Some of the 1,2-dichloropropane molecules were adsorbed more strongly than others and these molecules became even more strongly adsorbed in time. The fact that pulverization of the soil released a portion of the

chemical, suggests that the strongly adsorbed 1,2-dichloropropane eventually became occluded in the soil structure. Additionally, these observations suggest that the rate at which the chemical becomes occluded, or the adsorption coefficient increases, is diffusion-controlled.

The dissipation of 1,2-dichloropropane was determined in two clay and two sandy soils in closed systems following application at normal field rates (Van Dijk 1980). The mean dissipation rate was 0.013 day^{-1} (half-life 52 days), with the rate roughly twice as high in the sandy soil as in the clay soil. Additionally, the rate of volatilization increased by a factor of two for a 10°C increase in temperature. In another experiment in which 1,2-dichloropropane was mixed with 3 cm of soil in an open container, covered with 12 cm of soil and left outdoors, <1% of the chemical remained after 10 days (Roberts and Stoydin 1976). This loss was attributed to volatilization.

A bioconcentration factor (BCF) of 19 in fish has been estimated for 1,2-dichloropropane using linear regression equations with an estimated log Kow of 1.99 (EPA 1988b; Lyman et al. 1982). An experimental value for the bioconcentration factor of <10 has also been reported (Kawasaki 1980). Only for those chemical with BCF values greater than 500-1000 is bioconcentration considered to be important. Therefore, 1,2-dichloropropane would not be expected to bioconcentrate significantly in fish. When potatoes were grown in sandy loam soil that had been treated with a mixture of ^{14}C-labeled 1,2-dichloropropane and 1,3-dichloropropene 5 months before sowing, only 7 ppb of the radioactivity was found in the mature potatoes indicating minimal uptake of either of these chemicals (Roberts and Stoydin 1976).

5.3.2 Transformation and Degradation

5.3.2.1 Air

The primary mode of degradation in air is through reaction with photochemically-produced hydroxyl radicals by H-atom abstraction (Singh et al. 1982). Experimental determinations of the reaction rate yield a halflife of >23 days (Atkinson 1985), whereas theoretical estimates result in a half-life of 16 days (Atkinson 1985). Lacking a chromophore that absorbs radiation >290 nm, direct vapor phase photolysis would not be expected. Accordingly, no photolysis occurred when 1,2-dichloropropane was exposed to simulated sunlight for prolonged periods of time (Cohen et al. 1984).

5.3.2.2 Water

1,2-Dichloropropane is resistant to hydrolysis, with an estimated hydrolysis half-life of 25-200 wk (Cohen et al. 1984). Most studies indicated that 1,.2-dichloropropane is also resistant to biotransformation. There was no degradation in a semicontinuous activated sludge process in ten weeks even when the retention time was as long as 25 hr (Shell 1984). There is also no degradation in standard 4-week tests that simulate

biodegradability in environmental waters (Kawasaki 1980; Anonymous 1983). While >99% of 1,2-dichloropropane was lost in a wastewater treatment facility, the loss was attributed to stripping, rather than biodegradation (Kincannon et al. 1983).

5.3.2.3 Soil

Little or no degradation of 1,2-dichloropropane has been reported in soil. When 71 ppm of radiolabeled 1,2-dichloropropane was applied to a sandy loam and medium loam soil in closed glass containers and incubated for 20 weeks, <0.2% of the applied radioactivity was found in degradation products (Roberts and Stoydin 1976).

5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

5.4.1 Air

No levels of 1,2-dichloropropane in rural or remote areas of the U.S. have been reported in the literature. Samples collected in 397 urban/suburban areas of the country had a median concentration of 57 parts per trillion (ppt) and a range of 22 to 110 ppt (Brodzinsky and Singh 1982). Round-the-clock sampling for periods of 1-2 weeks in seven U.S. cities ranged from 21-78 ppt (Singh et al. 1982). Levels of some of the chemicals measured were highest at night or in the early morning, and lowest in the afternoon, although no mention of this fact was specifically directed to 1,2-dichloropropane. Only 2% of the 1,2-dichloropropane levels monitored at four sites by the California Air Monitoring Program were above the quantitation limit of 0.2 ppt, although one value recorded in Riverside was 1100 ppt (Shikiya et al. 1984). During rain events in Portland, Oregon, gas phase concentrations of 1,2-dichloropropane ranged from 4.4-8.4 ppt (Ligocki et al. 1985). Levels of 1,2-dichloropropane in industrial or source-related areas of the U.S. ranged (39 sites) from 0-130 ppt with 120 ppt median (Brodzinsky and Singh 1982). The average concentration during a 3-month survey of ten source-related sites in Philadelphia, PA, was 259 ppt (Sullivan et al. 1985). In EPA's Philadelphia Geographic Area Multimedia Pollutant Survey, average ambient 1,2-dichloropropane levels ranged from 40-740 ppt in various sections of the city and 7700-120,000 ppt downwind of the Northeast Water Pollution Control Plant (EPA 1986c). This plant had received discharges from the Rohm and Haas plant which produced ion exchange resins using 1,2-dichloropropane as a solvent. The data compiled by Brodzinsky and Singh (1982) has been reviewed and most of it is of good quality. More data has now been added to this National Ambient Volatile Organic Compounds Database bringing the number of monitoring data points to 714 (Shah and Heyerdahl 1988). With the addition of the new data, the overall median concentration of 1,2-dichloropropane is 22 ppt and the lower and upper quartile concentrations are 11 and 65 ppt. The median concentration of the suburban, urban, and source-dominated sites were 42 ppt, 11 ppt, and 1 ppt, respectively. The fact that the 1,2-dichloropropane concentrations are higher at the 'cleaner' sites may

indicate that the degradation rate is lower at these sites rather than that there are more 1,2-dichloropropane emissions at these sites. The concentration of hydroxyl radicals that are responsible for the photooxidation of 1,2-dichloropropane are generally lower in cleaner atmospheres than dirty ones (Winer et al. 1984). The fact that the addition of more recent data to the National Ambient Volatile Organic Compounds Database has lowered the median 1,2-dichloropropane concentration from 57 ppt to 22 ppt (Brodzinsky and Singh 1982; Shah and Heyerdahl 1988) suggests that the reduction in 1,2-dichloropropane use has had an effect on ambient air concentrations.

Traces of 1,2-dichloropropane were detected outside 2 of 9 homes at the Old Love Canal in Niagara Falls, N.Y. (Barkley et al. 1980), while 0.29 ppb was found in the ambient air in a household basement (Pellizzarri 1982). The same authors did not find any 1,2-dichloropropane at the Kin-But waste disposal site near Edison, N.J. Traces to 0.46 ppb of 1,2-dichloropropane were found in Iberville Parish, LA, where many organic chemical and producer, user, and storage facilities are located along the Mississippi River (Pellizzarri 1982).

While one of 1,2-dichloropropane's major uses was once as a soil fumigant, no air monitoring data could be located in the available literature for agricultural areas in which it was used.

5.4.2 Water

1,2-Dichloropropane has been identified in 1.6% of samples from 11 water utilities along the Ohio River at a level of 0.1 ppb (Ohio River Valley Sanitation Commission 1979). In a U.S. Groundwater Supply survey in which 945 water supplies derived from groundwater sources were tested, 13 supplies were positive for 1,2-dichloropropane, with a median and maximum concentrations of 0.9 and 21 ppb, respectively (Westrick et al. 1984). In an ongoing study of 575 community water systems using groundwater sources and approximately 19,000 non-community and private wells in Suffolk County, NY, 0.9% of the community water systems and 5.5% of the other wells contained 1,2-dichloropropane making it the 5th most common contaminant found there (Suffolk County 1983b; Zaki 1986). In 1982 the California State Water Resources Control Board started investigating the presence of 1,2-dichloropropane in wells (Cohen et al. 1986; Ali et al. 1986) because of its high mobility in soil and possible carcinogenicity and mutagenicity. They found the chemical in 75 wells in nine counties ranging up to 1200 ppb; 12 wells exceeded the State's action level of 10 ppb (Ali et al. 1986). It is worth noting that 3 contaminated wells in residential and residential/commercial areas of Suffolk County, NY with 1,2-dichloropropane levels of 13-550 ppb were in areas where agricultural use was claimed not to be a source of contamination (Suffolk County 1983a). 1,2-Dichloropropane was found in at least 7 shallow wells in western Washington associated with soil injection in strawberry fields (Cohen et al. 1986). Nine out of 20 samples of groundwater underlying landfills in Minnesota contained 0.5-43

ppb of 1,2-dichloropropane (Sabel and Clark 1984). In a separate Minnesota landfill study, 1.5-7.6 ppb of 1,2-dichloropropane was found in the groundwater underlying a landfill in a sand plain that was known to have received industrial waste, but was absent from the boring taken directly above the contaminated groundwater; while 1.1 ppb of 1,2-dichloropropane was found in the groundwater from a clay landfill in southwestern Minnesota (Sabel and Clark 1984).

1,2-Dichloropropane has been found in major rivers of the United States; up to 20% of the samples from monitoring studies contained from trace quantities to >l0 ppb of the chemical (Kaiser et al. 1983; Ohio River Valley Water Sanitation Commission 1980; Ohio River Valley Water Sanitation Commission 1982). Of the 95 stations monitored in Lake Ontario, 4 had concentrations ranging from 210-440 ppt and 15 others had trace quantities, while in 16 stations in the Lower Niagara River, 4 stations had concentrations ranging from 7-55 ppt, while 5 other stations had trace quantities (Kaiser et al. 1983). Of the 4972 samples at 11 stations on the Ohio River monitored in 1980-81, 8.8% were positive, with 28 samples between l-10 ppb and 1 sample contained >10 ppb (Ohio River Valley Water Sanitation Commission 1982). Between 1980 and 1988, 29,320 samples of surface water in EPA's STORET database were analyzed for 1,2-dichloropropane (STORET 1988). Ten percent of the samples were 0.40 parts per billion (ppb) or higher with a maximum level of 300 ppb. In addition, of the 859 sediment analyzed, 10% contained 1,2-dichloropropane above 44 ppb. Of the 22,457 samples of groundwater in the database, 10% were above 3 ppb and the maximum was 1500 ppb.

5.4.3 Soil

1,2-Dichloropropane was present in concentrations up to 12.2 ppb in soil cores underlying a recently fumigated field in California (Ali et al. 1986). In another California study, it was found at 0.2-2.2 ppb in soil cores up to 7 meters below the surface (Cohen et al. 1984). Some unspecified samples of soil, water, or sediment from the Love Canal contained unspecified amounts of 1,2-dichloropropane (Hauser and Bromberg 1982). 1,2-Dichloropropane was found at nine of the 951 hazardous waste sites listed on the National Priority List (NPL) of highest priority sites for possible remedial action (ATSDR 1988). Runoff and soil and groundwater contamination with 1,2-dichloropropane was reported at these sites. Additionally, it was found in 5 sites in the Contract Laboratory Statistical Database at median concentrations ranging from 6.5 to 23,000 ppb (Viar and Company 1987).

5.4.4 Other Media

No documentation of 1,2-dichloropropane in flora or fauna in the U.S. was located.

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5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

A National Occupational Exposure Survey (NOES) conducted by NIOSH from 1981 to 1983 estimated that 2119 workers including 949 women were potentially exposed to 1,2-dichloropropane in the United States (NIOSH 1988). The distribution of these estimated exposed workers by standard industrial category (SIC) was: 408 in business services, 831 in machinery, except electrical, 161 in fabricated metal products, 672 in the chemical and allied products, and 47 in textile mill products. The estimate was provisional as all of the data for trade name products which may contain 1,2-dichloropropane has not been analyzed. The NOES was based on field surveys of 4490 facilities and was designed as a nationwide survey based on a statistical sample of virtually all workplace environments in the United States where eight or more persons were employed in all SIC codes except mining and agriculture. The use pattern of 1,2-dichloropropane has changed radically since the survey was made, as it has been eliminated from agricultural fumigants, photographic film manufacture, and paint strippers. The results of the NOES, even though it excludes agricultural workers, are expected to be high. Another category of worker that may be exposed to 1,2-dichloropropane are workers at wastewater treatment facilities that handle effluent containing this chemical. Volatilization would be expected during treatment operations. According to Dow Chemical Company, the major manufacturer of 1,2-dichloropropane, all processes involving the production, conversion, and disposal of 1,2-dichloropropane are closed process (Dow Chem. Co. 1983). By their estimates, 45 and 123 workers are routinely and potentially exposed, respectively, to the chemical (Dow Chem. Co. 1983). The levels of exposure they report are <2 ppm for toluene diisocyanate (TDI) production, <l ppm in ion exchange resin manufacture, and <25 ppm in paper coating (Dow Chem. Co. 1983).

According to drinking water surveys (Ali et al. 1986; Cohen et al. 1986; Ohio River Valley Sanitation Commission 1979; Westrick et al. 1984; Zaki 1986), a significant number of drinking water supplies contained 1,2-dichloropropane and people drinking this water would have been exposed to this chemical. In the most broadly-based groundwater survey, 1.4% of these supplies contained median water concentrations of 0.9 parts per billion (ppb) (Westrick et al. 1984). People drinking this water would ingest 1.8 c(g of 1,2-dichloropropane per day. While most of the drinking supplies tested for 1,2-dichloropropane were taken from groundwater sources, in cities such as Philadelphia, PA which obtains its water from a river that received sizeable amounts of 1,2-dichloropropane-containing effluent, the concentration of 1,2-dichloropropane in the drinking water from the Baxter Drinking Water Plant averaged 1.5 ppb (EPA 1986). People consuming this water would have ingested 3.0 μg of 1,2-dichloropropane daily.

The general population is exposed to 1,2-dichloropropane in ambient air, which contains median 1,2-dichloropropane levels of 22 ppt which translates into a daily intake of 2.1 μg. Residents of Philadelphia, according to EPA's Philadelphia Geographic Area Multimedia Pollutant Survey,

would have been exposed to much higher inhalation doses, 98-660 µg/day because a large user of 1,2-dichloropropane was located there (EPA 1986c). People living in the vicinity of landfills containing 1,2-dichloropropane may be exposed to 1,2-dichloropropane present in landfill gases. Not enough information is available to estimate what the level of exposure from this source might be. Subsurface and surface emissions of volatile organic compounds (VOCs) have been found from RCRA Subtitle D disposal sites which reportedly received only non-hazardous waste. However, hazardous waste from small quantity generators or household hazardous waste may be disposed of at these landfills. For landfills that are similar in design and content, emissions are estimated to be a factor of 2.6 greater in a wet climate than in a dry one (Vogt et al. 1987)

5.6 POPULATIONS WITH POTENTIALLY HIGH EXPOSURE

Those people consuming contaminated drinking water will have the greatest potential for exposure to significant levels of 1,2-dichloropropane. Since the odor threshold for 1,2-dichloropropane is 10 ppb (Amoore and Hautala 1983), people consuming water with this level of 1,2-dichloropropane may have a warning that their water is contaminated. In general, drinking water supplies that are most apt to be contaminated are those taken from groundwater sources. Contaminated drinking water wells are most likely to be found in agricultural areas with sandy soil where the chemical was used as a fumigant. However, there are special situations, such as in Philadelphia, where drinking water derived from surface water sources may be contaminated with 1,2-dichloropropane-containing effluent. In Philadelphia, 1,2-dichloropropane-containing effluent from an industrial plant was driven upstream to the influent of a drinking water plant by tidal action. This plant recently discontinued using 1,2-dichloropropane. People residing in the vicinity of industrial sources may be exposed to 1,2-dichloropropane in the ambient air, either from direct emissions or volatilization of the chemical from wastewater.

5.7 ADEQUAGY OF THE DATABASE

Section 104 (i) (5) of CERCLA, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of 1,2-dichloropropane is available. Where adequate information is not available, ATSDR, in cooperation with the National Toxicology Program (NTP), is required to assure the initiation of a program of research designed to determine these health effects (and techniques for developing methods to determine such health effects). The following discussion highlights the availability, or absence, of exposure and toxicity information applicable to human health assessment. A statement of the relevance of identified data needs is also included. In a separate effort, ATSDR, in collaboration with NTP and EPA, will prioritize data needs across chemicals that have been profiled.

5. POTENTIAL FOR HUMAN EXPOSURE

5.7.1 Data Needs

Physical and Chemical Properties. The physical and chemical properties of 1,2-dichloropropane have been adequately characterized (see table 3.2).

Environmental Fate. Sufficient data exists to show that chemical hydrolysis and aerobic biodegradation of 1,2-dichloropropane are very slow and are not significant in determining the half-life in surface water or soil. No experimental studies of anaerobic biotransformation are available; these could be useful in estimating the half-life of 1,2-dichloropropane in soil and groundwater. Experimental hydrolysis data at pH 5-9 would be helpful for predicting the half-life of 1,2-dichloropropane in groundwater where volatilization is not significant.

Exposure Levels in Environmental Media. Since 1,2-dichloropropane was phased out as a fumigant and its use in solvents has declined, recent monitoring data are needed for air, groundwater, and surface water. This is particularly important with respect to groundwater, where it is especially long-lived and may be present in significant concentrations. Field monitoring studies of 1,2-dichloropropane would also be useful. This may be the only feasible way of determining the half-life of 1,2-dichloropropane in groundwater. Air monitoring and surface water studies would show the effects of changing 1,2-dichloropropane use patterns. While EPA's Storet database contains considerable water.monitoring data, there are problems with the database that limit its usefulness. The detection limit is apparently recorded when no chemical is detected, so that it is impossible to say whether the 90 percentile figures for surface water and groundwater quoted in Section 5.4.2 represent positive determinations or merely detection limits. It would be helpful if this monitoring data would indicate whether 1,2-dichloropropane was actually detected in the samples.

Exposure Levels in Humans. The use pattern of 1,2-dichloropropane has changed radically since NIOSH's National Occupational Exposure Survey (NOES). Since the elimination of 1,2-dichloropropane from agricultural fumigants, photographic film manufacture, and paint strippers, fewer workers are exposed. While agricultural workers were not included in the survey, those engaged in the manufacture of agricultural chemicals were included. As a chemical in paint strippers, 1,2-dichloropropane would have a particularly high potential for exposing large numbers of people at high levels of exposure, since such applications are labor intensive and performed in the open. Therefore the results of the NOES will have to be reanalyzed in light of current use patterns in order to reflect current occupational exposures.

Exposure Registries. Other than the NIOSH survey, no exposure registries for 1,2-dichloropropane were located. The development of a registry of exposed persons would provide a useful reference tool in assessing exposure levels and frequency. In addition, a registry would

allow an assessment of the variations in exposure concentrations by, for example, geography, season, regulatory actions, presence of hazardous waste landfills, or manufacturing or use facility. These assessments, in turn, would provide a better understanding of the needs for some types of research or data acquisition based on the current exposure concentrations. Additionally, such a database of exposures may be useful for linking exposure to 1,2-dichloropropane with specific toxic effects or diseases.

5.7.2 On-going Studies

No on-going monitoring studies or studies relating to the environmental fate of 1,2-dichloropropane were located in the available literature.

According to Emergency Planning and Community Right to Know Act of 1986 (EPCRTKA), (§313), (Pub. L. 99-499, Title III, §313), industries are required to submit release information to the EPA. The Toxic Release Inventory (TRI), which contains release information for 1987, became available in May of 1989. This database can be updated yearly and should provide a more reliable estimate of industrial production and emissions, which will be useful for determining potential human exposure.

NIOSH is continuing to revise its estimates of occupational exposures in its National Occupational Exposure Survey (NOES) through the inclusion of trade name compounds. As part of the Third National Health and Nutrition Evaluation Survey (NHANES III), the Environmental Health Laboratory Sciences Division of the Center for Environmental Health and Injury Control, Centers for Disease Conrol, will be analyzing human blood samples for 1,2-dichloropropane and other volatile organic compounds. These data will give an indication of the frequency of occurrence and background levels of these compounds in the general population.

6. ANALYTICAL METHODS

6.1 BIOLOGICAL MATERIALS

The analytical methods for the determination of 1,2-dichloropropane in biological matrices are given in Table 6-l. The purge and trap method used for environmental samples is also commonly used for biological samples. The discussion about the methods that may be most sensitive for the determination of 1,2-dichloropropane levels in environmental samples, the advantages and disadvantages of the commonly used methods, and the precautions required to avoid evaporation losses as given in Subsection 6.2 is also applicable for biological samples.

6.2 ENVIRONMENTAL SAMPLES

As with all extremely volatile chemicals, it is essential to take precautions during sampling, storage, and analysis to avoid loss of 1,2-dichloropropane. Analytical methods for determining 1,2-dichloropropane in environmental samples are presented in Table 6-2. The two common methods that are used for the preconcentration of 1,2-dichloropropane for the determination of its levels in air are adsorption on a sorbent column or collection in a cryogenically-cooled trap, although the use of oxygen-doped electron capture detection may eliminate the need for preconcentration (Rasmussen et al. 1980). The disadvantages of cryogenic cooling are that the method is cumbersome and that condensation of moisture in air may block the passage of further air flow through the trap. The disadvantages of the sorption tubes are that the sorption and desorption efficiencies may not be 100% and that the background impurities in the sorbent tubes may limit the detection limit for samples at low concentrations (Cox 1983).

The most common method for the determination of 1,2-dichloropropane levels in water, sediment, soil and aquatic species is the purging of the vapor from the sample or its suspension in water with an inert gas and trapping the desorbed vapors in a sorbent trap. Subsequent thermal desorption is used for the quantification of its concentration.

The two methods that provide the lowest detection limits are halide-specific detectors (e.g., Hall electrolytic conductivity detector) and mass spectrometer. The advantage of halide specific detectors are they are not only very sensitive but are also specific for halide compounds. The mass spectrometer, on the other hand, provides an additional confirmation of the presence of a compound through the ionization patterns and is desirable when a variety of compounds are required to be quantified. The disadvantage of halide-specific detectors for their inability to detect and quantify nonhalogen compounds can be greatly overcome by using other detectors (e.g., photoionization detector) in series (Lopez-Avila et al. 1987; Driscoll et al. 1987). High-resolution gas chromatography with capillary columns is a better method for volatile compounds than packed columns because they provide better resolution of closely eluting compounds and increase the

TABLE 6-1. Analytical Methods for 1,2-Dichloropropane in Biological Samples

Sample Matrix	Sample Preparation	Analytical Method	Detection Limit	Accuracy	Reference
Exhaled air	exhaled air collected by valved Teflon Spriometer mouth pieces into Tedlar bag. The content of bag sorbed in Tenax and thermally desorbed	cryofocussing HRGC-MS	NG	NG	Barkely et al., 1980
Blood and urine	sample mixed with water purged at 50°C, trap in Tenax, thermal desorption	cryofocussing HRGC-MS	NG	NG	Barkely et al., 1980
Blood	sample mixed with water purged at ambient temperature and trapped in Tenax and thermally desorbed	GC-MS	<100 ppt	55-60% at 1 ppb	Cramer et al., 1988
Urine	sample equilibrated in sealed in vial at 37°C and head space gas analyzed	HRGC-MS	NG	NG	Ghittori et al., 1987

NG - Not given; GC - gas chromatography; HRGC - high resolution gas chromatography; MS - mass spectrometry

TABLE 6-2. Analytical Methods for 1,2-Dichloropropane in Environmental Samples

Sample Matrix	Sample Preparation	Analytical Method	Detection Limit	Accuracy	Reference
Ambient air	aliquot of sample collected in Tedlar bag, concentrated in a cryogenic trap and thermally disolved	GC-ECD	0.2 ppb	NG	Shikiya et al. 1984
Ambient air	aliquot of sample collected in electropolished cylinder cryogenically preconcentrated	GC-ECD	4 ppt	85-115%	Singh et al. 1982
Indoor/Outdoor air	sample collected by adsorption through charcoal desorbed by CS_2	HRGC-ECD	10 ppb	NG	DeBortoli et al. 1986
Occupational air	sample collected by adsorption on charcoal, desorbed in acetone/ cyclohexane	GC-HELD	33 $\mu g/m^3$ (7 ppb)	<95%	NIOSH 1984; *Boyd et al.* 1981; Dillon 1981
Air from industrial and chemical water disposal sites	sample collected by adsorption on Tenax, thermally desorbed	cryofocussing HRGC-MS	<0.2 $\mu g/m^3$ (<0.04 ppb)	>75%	Pellizzani 1982
Finished drinking and raw source water	purge and trap, thermal desorption	GC-MS	<0.1 µg/L (0.1 ppb)	90%	Otson 1987
	purge at ambient temperature, trap in Tenax/Silica/Charcoal and desorb thermally	GC-HEED (EPA Method 502.1)	NG	95% at 0.4 µg/L	EPA 1986a
	purge and ambient temerature, trap in Tenax/Silica/Charcoal desorb thermally	subambient programmable GC-NC (EPA Method 524.1)	0.17 µg/L (0.17 ppb)	101% 1 µg/L	EPA 1986a
	purge at ambient temperature, trap in Tenax/Silica/Charcoal, thermally desorbed	cryofocussing (wide or HRGC-MS (EPA-Method 524.2)	0.04 µg/L (wide bore) 0.02 µg/L (narrow bore)	97% (wide bore) at 0.1-10 µg/L 96% (narrow bore) at 0.5 µg/L	EPA 1986a
Drinking/ground/ surface water	vacuum distillation with cryogenic trapping	HRGC-ECD	0.03 µg/L	81%	Comba and Kaiser 1983
Water/waste-water	purge at ambient temperature, trap in Tenax/Silica/Charcoal, thermally	GC-HECD (EPA Method 601)	0.04 µg/L	97.7% at 0.29-39.0 µg/L	EPA 1982a

TABLE 6-2 (continued)

Sample Matrix	Sample Preparation	Analytical Method	Detection Limit	Accuracy	Reference
Water/wastewater	purge at ambient temperature, trap in Tenax/Silica/Charcoal, thermally	GC-HECD (EPA Method 601)	0.04 µg/L	97.7% at 0.29-39.0 µg/L	EPA 1982a
Wastewater	purge at ambient temperature, trap in Tenax/Silica thermally desorb	GC-MS (EPA Method 624)	6 µg/L	102-103%	EPA 1982a
Groundwater/ leachate	purge at ambient temperature, trap in Tenax/Silica, desorb thermally	GC-MS (EPA-CLP method)	5 µg/L	NG	EPA 1987a
Water and fish	dry purge and trap (water), somicated fish slurry subjected to dry purge and trap	cryofocussing HRGC-HECD/ PID in series	NG	NG	Driscall et al. 1986
Sediment/fish	vacuum distillation and condensation in supercooled trap	HRGC-MS	NG	96% (sediment) 54% (fish)	Hiatt 1981; Hiatt 1983
Marine biota/ sediment	homogenized ultrasonically (fish) or water suspension (sediment) sample purged at 70°C, trapped in Tenax/Silica and thermally desorbed	cold focussing HRGC-MS	<0.2 µg/kg	NG	Ferrario et al. 1985
Fish	cut tissue purged at 50°C, trap in charcoal desorb in CS_2	HRGC-FID	NG	61%	Reinert et al. 1983
Soil/sediment	purge sample suspension in water at 50°C, trap in Tenax/Silica, thermally desorb	GC-MS (EPA-CLP method)	5 µg/kg	NG	EPA 1987a
Liquid and solid waste	solid samples dispersed in a glycol, purge at ambient temperature, trap in Tenax/silica, desorb thermally	GC-HELD (EPA methods 5030 and 8010)	0.4 µg/L (groundwater) 0.4 µg/L (soil) 20 µg/Kg (liquid waste) 50 µg/kg (soil and sludge)	44-156%	EPA 1982b, EPA 1986b
Groundwater, solid waste, or sludge	sample disposed in a glycol, purged at ambient temperature, trapped in	GC-HELD and PID in Series	1-5 µg/g (for soil)	80% (groundwater)	Lopez-Avila et al. 1987

NG - not given; GC - gas chromatography; MS - mass spectrometry; HRGC - high resolution gas chromatography; HEED - hall electrolytic conductivity detector; PID - photoionization detector; ECD - electron capture detector; FID - flame ionization detector

sensitivity of detection. In addition, purge and whole column cryotrapping eliminates the need for the conventional purge and trap unit and reduces the time of analysis (Pankow and Rosen 1988). The plugging of the trap by the condensation of moisture during cryotrapping may be avoided by the use of very wide bore capillary column, although the chromatographic resolution of such a column is inferior to narrow bore capillary columns (Pankow and Rosen 1988; Mosesman et al. 1987).

6.3 ADEQUACY OF THE DATABASE

Section 104 (i) (5) of CERCLA, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of 1,2-dichloropropane is available. Where adequate information is not available, ATSDR, in cooperation with the National Toxicology Program (NTP), is required to assure the initiation of a program of research designed to determine these health effects (and techniques for developing methods to determine such health effects). The following discussion highlights the availability, or absence, of exposure and toxicity information applicable to human health assessment. A statement of the relevance of identified data needs is also included. In a separate effort, ATSDR, in collaboration with NTP and EPA, will prioritize data needs across chemicals that have been profiled.

6.3.1 Data Needs

Methods for Determining Parent Compounds and Metabolites in Biological Materials. The analytical methods for determining volatile chlorinated hydrocarbon levels in biological matrices are quite general. However, there is a paucity of data specific to 1,2-dichloropropane. The limited number of publications that discuss the methods for the determination of this compound in biological matrices do not report either the recovery or the detection limit of the compound in different biological matrices. The study of the levels of the parent compound in human blood, urine or other biological matrices can be useful in deriving a correlation between the level of this compound found in the environment and those found in the body. One study (Ghittori et al. 1987) reported that a correlation exists between the urinary level and the TWA level of 1,2-dichloropropane measured at the breathing zone. No metabolite of 1,2-dichloropropane from human exposure to this compound has yet been identified, although specific metabolites have been identified in the urine of rats (see Subsection 2.6.3). The changes in metabolite concentrations with time in human blood, urine, or other appropriate biological medium may be useful in estimating its rate of metabolism in humans. In some instances, metabolite levels may be useful in correlating exposed doses to human body burdens. Such studies on the levels of metabolites in human biological matrices are not available for this compound.

6. ANALYTICAL METHODS

Methods for Biomarkers of Exposure. No biomarker of exposure to 1,2-dichloropropane has been identified (see Subsection 2.9.2). If a biomarker for this compound in a human biological tissue or fluid were available and 'a correlation were found to exist between the level of biomarker and a certain health effect, it could be used as an indication of a health effect caused by the exposure to this chemical.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. Analytical methods are available for the quantification of 1,2-dichloropropane in environmental samples. The levels of this compound in different environmental media can be used to indicate exposure of 1,2-dichloropropane to humans through the inhalation of air and ingestion of drinking water and foods containing 1,2-dichloropropane. If a correlation with human tissue or body fluid levels was found to exist, the intake levels from different environmental sources could be used to estimate the body burden of the chemical in humans. Although the products resulting from the biotic or abiotic degredation of 1,2-dichloropropane in the environment can be inferred, there has been no systematic study of the concentrations of these reaction products in the environment. In instances where the product(s) of an environmental reaction is more toxic than the parent compound, it is important that the level of the degradation products in the environment be known. No such reaction products have been identified for 1,2-dichloropropane. Analytical methods are available for the quantification of the known reaction products of 1,2-dichloropropane in the environment.

6.3.2 On-going Studies

The Environmental Health Laboratory Sciences Division of the Center for Environmental Health and Injury Control, Centers for Disease Control, is developing methods for the analysis of 1,2-dichloropropane and other volatile organic compounds in blood. These methods use purge and trap methodology and magnetic mass spectrometry which gives detection limits in the low parts per trillion range.

7 . REGULATIONS AND ADVISORY STANDARDS

National and state regulations and guidelines pertinent to human exposure to 1,2-dichloropropane are summarized in Table 7-l.

The Clean Water Effluent Guidelines regulate 1,2-dichloropropane for the following industrial point sources: electroplating, organic chemicals, steam electric, asbestos, timber products processing, metal finishing, paving and roofing, paint formulating, ink formulating, gum and wood, and carbon black (EPA 1988).

7. REGULATIONS AND ADVISORY STANDARDS

TABLE 7-1. Regulations and Guidelines Applicable to 1,2-Dichloropropane

Agency	Description	Value	Reference
	International		
IARC	Cancer Classification	Group 3[a]	IARC 1987 Supp 7
	National		
Regulations			
Air			
OSHA	Permissible Exposure Limit	75 ppm	OSHA 1989
	Short-Term Exposure Limit	110 ppm	
Non-Specific Media			
EPA OERR	Reportable Quantity	1000 lbs	EPA 1986d
Guidelines			
Air			
ACGIH	Threshold Limit Value		
	Time-Weighted-Average	75 ppm	ACGIH 1987
	Short Term Exposure Limit	110 ppm	ACGIH 1987
Other			
EPA	q_1* for Oral Exposure (proposed)	0.068(mg/kg/day)$^{-1}$	EPA 1987b
EPA	Cancer Classification	Group B2[b]	EPA 1987b
	State		
State Agencies	Drinking Water quality guidelines		FSTRAC 1988
Arizona		1 µg/L	
California		10 µg/L	
Connecticut		10 µg/L	
Kansas		6 µg/L	
Maine		1 µg/L	
Minnesota		6 µg/L	
Massachusetts		0.001 mg/L	MAORS 1989
	Acceptable ambient air concentrations		NATICH 1987
Connecticut		100 µg/m^3 (8-hr avg)	
Kansas		13.89 µg/m^3 (annual avg)	
Maine		5.1 µg/m^3 (24-hr avg)	
Nevada		8.33 mg/m^3 (8-hr avg)	
Virginia		5800 µg/m^3 (24-hr avg)	

[a]Agent is not classifiable as to its carcinogenicity in humans.
[b]Probable human carcinogen.

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9. GLOSSARY

Acute Exposure -- Exposure to a chemical for a duration of 14 days or less, as specified in the Toxicological Profiles.

Adsorption Coefficient (K_{oc}) -- The ratio of the amount of **a** chemical adsorbed per unit weight of organic carbon in the soil or sediment to the concentration of the chemical in solution at equilibrium.

Adsorption Ratio (K_d) -- The amount of a chemical adsorbed by a sediment or soil (i.e., the solid phase) divided by the amount of chemical in the solution phase, which is in equilibrium with the solid phase, at a fixed solid/solution ratio. It is generally expressed in micrograms of chemical sorbed per gram of soil or sediment.

Bioconcentration Factor (BCF) -- The quotient of the concentration of a chemical in aquatic organisms at a specific time or during a discrete time period of exposure divided by the concentration in the surrounding water at the same time or during the same time period.

Cancer Effect Level (CEL) -- The lowest dose of chemical in a study or group of studies which produces significant increases in incidence of cancer (or tumors) between the exposed populaton and its appropriate control.

Carcinogen -- A chemical capable of inducing cancer.

Ceiling Value (CL) -- A concentration of a substance that should not be exceeded, even instantaneously.

Chronic Exposure -- Exposure to a chemical for 365 days or more, as specified in the Toxicological Profiles.

Developmental Toxicity -- The occurrence of adverse effects on the developing organism that may result from exposure to a chemical prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism.

Embryotoxicity and Fetotoxicity -- Any toxic effect on the conceptus as a result of prenatal exposure to a chemical; the distinguishing feature between the two terms is the stage of development during which the insult occurred. The terms, as used here, include malformations and variations, altered growth, and in utero death.

EPA Health Advisory -- An estimate of acceptable drinking water levels for a chemical substance based on health effects information. A health advisory is not a legally enforceable federal standard, but serves as technical guidance to assist federal, state, and local officials.

9. GLOSSARY

Immediately Dangerous to Life or Health (IDLH) -- The maximum environmental concentration of a contaminant from which one could escape within 30 min without any escape-impairing symptoms or irreversible health effects.

Intermediate Exposure -- Exposure to a chemical for a duration of 15-364 days, as specified in the Toxicological Profiles.

Immunologic Toxicity -- The occurrence of adverse effects on the immune system that may result from exposure to environmental agents such as chemicals.

In vitro -- Isolated from the living organism and artificially maintained, as in a test tube.

In vivo -- Occurring within the living organism.

Lethal Concentration$_{(LO)}$ (LC_{LO}) -- The lowest concentration of a chemical in air which has been reported to have caused death in humans or animals.

Lethal Concentration$_{(50)}$ (LC_{50}) -- A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

Lethal Dose$_{(LO)}$ (LD_{LO}) -- The lowest dose of a chemical introduced by a route other than inhalation that is expected to have caused death in humans or animals.

Lethal Dose$_{(50)}$ (LD_{50}) -- The dose of a chemical which has been calculated to cause death in 50% of a defined experimental animal population.

Lowest-Observed-Adverse-Effect Level (LOAEL) -- The lowest dose of chemical in a study or group of studies which produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

LT_{50} (lethal time) -- A calculated period of time within which a specific concentration of a chemical is expected to cause death in 50% of a defined experimental animal population.

Malformations -- Permanent structural changes that may adversely affect survival, development, or function.

Minimal Risk Level (MRL) -- An estimate of daily human exposure to a chemical that is likely to be without an appreciable risk of deleterious effects (noncancerous) over a specified duration of exposure.

9. GLOSSARY

Mutagen -- A substance that causes mutations. A mutation is a change in the genetic material in a body cell. Mutations can lead to birth defects, miscarriages, or cancer.

Neurotoxicity -- The occurrence of adverse effects on the nervous system following exposure to a chemical.

No-Observed-Adverse-Effect Level (NOAEL) -- That dose of chemical at which there are no statistically or biologically significant increases in frequency or severity of adverse effects seen between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

Octanol-Water Partition Coefficient (K_{ow}) -- The equilibrium ratio of the concentrations of a chemical in n-octanol and water, in dilute solution.

Permissible Exposure Limit (PEL) -- An allowable exposure level in workplace air averaged over an 8-h shift.

q_1* -- The upper-bound estimate of the low-dose slope of the dose-response curve as determined by the multistage procedure. The q_1* can be used to calculate an estimate of carcinogenic potency, the incremental excess cancer risk per unit of exposure (usually g/L for water, mg/kg/day for food, and g/m^3 for air).

Reference Dose (RfD) -- An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure of the human population to a potential hazard that is likely to be without risk of deleterious effects during a lifetime. The RfD is operationally derived from the NOAEL (from animal and human studies) by a consistent application of uncertainty factors that reflect various types of data used to estimate RfDs and an additional modifying factor, which is based on a professional judgment of the entire database on the chemical. The RfDs are not applicable to nonthreshold effects such as cancer.

Reportable Quantity (RQ) -- The quantity of a hazardous substance that is considered reportable under CERCLA. Reportable quantities are: (1) 1 lb or greater or (2) for selected substances, an amount established by regulation either under CERCLA or under Sect. 311 of the Clean Water Act. Quantities are measured over a 24-h period.

Reproductive Toxicity -- The occurrence of adverse effects on the reproductive system that may result from exposure to a chemical. The toxicity may be directed to the reproductive organs and/or the related endocrine system. The manifestation of such toxicity may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of this system.

9. GLOSSARY

Short-Term Exposure Limit (STEL) -- The maximum concentration to which workers can be exposed for up to 15 min continually. No more than four excursions are allowed per day, and there must be at least 60 min between exposure periods. The daily TLV-TWA may not be exceeded.

Target Organ Toxicity -- This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular) .extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical.

TD_{50} (toxic dose) -- A calculated dose of a chemical, introduced by a route other than inhalation, which is expected to cause a specific toxic effect in 50% of a defined experimental animal population.

Teratogen -- A chemical that causes structural defects that affect the development of an organism.

Threshold Limit Value (TLV) -- A concentration of a substance to which most workers can be exposed without adverse effect. The TLV may be expressed as a TWA, as a STEL, or as a CL.

Time-weighted Average (TWA) -- An allowable exposure concentration averaged over a normal 8-h workday or 40-h workweek.

Uncertainty Factor (UF) -- A factor used in operationally deriving the RfD from experimental data. UFs are intended to account for (1) the variation il sensitivity among the members of the human population, (2) the uncertainty in extrapolating animal data to the case of humans, (3) the uncertainty in extrapolating from data obtained in a study that is of less than lifetime exposure, and (4) the uncertainty in using LOAEL data rather than NOAEL data. Usually each of these factors is set equal to 10.

APPENDIX: PEER REVIEW

A peer review panel was assembled for 1,2-dichloropropane. The panel consisted of the following members: Dr. William Lappenbusch, Toxicologist, Lappenbusch Environmental Health, Inc.; Dr. Hugh Farber, Private Consultant, Farber Associates; Dr. Carson Conaway, Research Scientist, Naylor Dana Institute; and Dr. Richard Carchman, Associate Professor, Toxicology and Pharmacology, Medical College of Virginia. These experts collectively have knowledge of 1,2-dichloropropane's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in the Superfund Amendments and Reauthorization Act of 1986, Section 110.

A joint panel of scientists from ATSDR and EPA has reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply their approval of the profile's final content. The responsibility for the content of this profile lies with the Agency for Toxic Substances and Disease Registry.

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